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Three officers of the newly formed Inter-Society Committee for a National Science Foundation. Left to right: Harlow Shapley, president, AAAS vice-Chairman; Edmund E. Day, president, Cornell University, chairman; and Dael Wolfle, executive secretary, American Psychological Association, secretary-treasurer (*Science*, February 28). The entire Executive Committee met in Washington on March 5. President Day testified before the Committee on Interstate and Foreign Commerce of the House of Representatives on March 6, explaining the position of the new group with respect to the proposed legislation before Congress (*News and Notes*).

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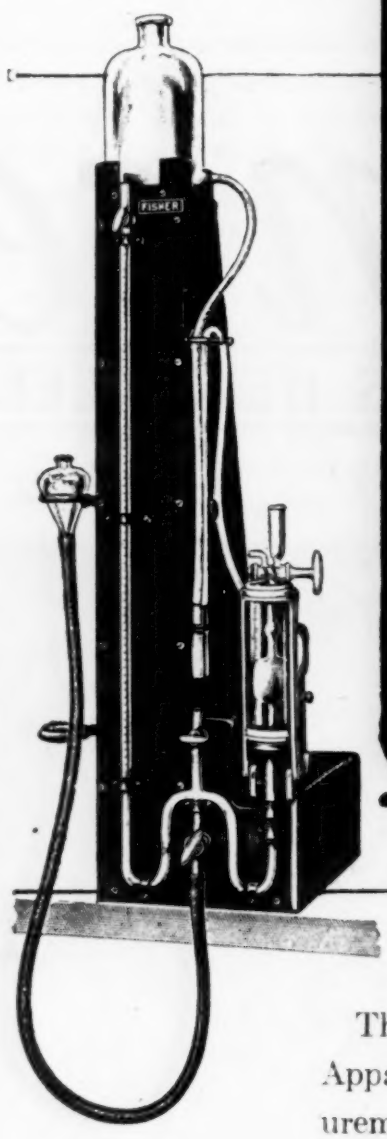
The Chemical Production of Mutations

C. Auerbach, J. M. Robson, and J. G. Carr



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The Chemical Production of Mutations

C. Auerbach, J. M. Robson, and J. G. Carr

Institute of Animal Genetics and *Department of Pharmacology, University of Edinburgh*

A GENETIC MUTATION IS A CHANGE, presumably chemical in nature, in one of the genes which compose the chromosome thread. The mutated gene is as stable as the original; it goes on reproducing replicas of its mutated self and thus initiates a new hereditary line. It is believed that without mutation life would never have proceeded beyond its very first elementary beginnings. Yet the mechanism of this important process is practically unknown. With the discovery by H. J. Muller (*12*) that mutations can be produced artifically by X-rays, a new approach to the problem of mutation was opened up, and many new facts relating to this problem were brought to light. One of the most important results was the discovery that the term "mutation" includes a number of distinct processes. In addition to gene mutations as defined above, X-rays produce breaks in the chromosome threads; when the resulting fragments join together in novel combinations, so-called chromosome rearrangements, hereditary changes closely resembling mutations may be produced. Rules connecting quantity and quality of radiation with type and frequency of mutations were discovered, and inferences could be drawn on number of ionizations required, size of the sensitive gene volume, etc. (*10*). Yet the actual processes of gene mutation and chromosome breakage—if indeed these are essentially different from one another—are still as mysterious as ever.

X-rays are destructive and nondiscriminating. It is conceivable that less severe methods of producing mutations might make possible a closer insight into the processes concerned. An advance in this direction was made when it was found that ultraviolet light, too, is capable of producing mutations. The restriction of the effective wave length to a comparatively narrow range which includes the absorption bands of nucleic acid and certain protein components supported the hypothesis, put forward by radiation geneticists, that the first step toward the production of a mutation consists in the absorption of an energy quantum by some constituent of the chromosome. But the hope that more specific effects, dependent on the wave length, might be produced, was not realized. Certain differences between the action of ultraviolet and that of the much shorter waves of X- and gamma rays are not yet understood, but may eventually prove helpful in the analysis of the mutation process (*18*).

Chemical substances with mutagenic properties should be particularly useful tools for attacking the problems of mutation. If, as we assume, a mutation is a chemical process, then knowledge of the reagents capable of initiating this process should throw light not only on the reaction itself, but also on the nature of the gene, the other partner in the reaction. Moreover, it could be hoped that among chemical mutagens there might be some with particular affinities for individual genes. Detection of such substances not only would be of high theoretical interest but would also open up the long-sought-for way to the production of directed mutations.

The search for chemical mutagens has been going on for well over 20 years. The choice of substances tried for the purpose was mainly random. Iodine, ammonia, metal compounds, and carcinogens are only some out of the great number tested. Results were often clearly negative, and no clearly positive ones had been obtained up to the beginning of our experiments in 1940 (see *1*, *9*, *19*). It is obvious that a chemical mutagen must possess very special properties. It must be able to act selectively on the genic material without at the same time destroying the cell which contains this material. It was, therefore, only to be expected that many substances would have to be tried before an effective one was found, and the search was continued by many workers. This search was encouraged by the accumulation of data which pointed to an influence of physiological conditions, such as age (*13*), sex (*1*), starvation (*15*), and of the genotype itself (*5*, *11*, *16*) on mutation rate. If, thus, chemical conditions created by the organism itself are capable of influencing the process of mutation, it did not seem beyond hope that chemical substances introduced from outside might have similar effects.

The choice of mustard gas for trials of this kind was suggested by observations pointing to its interference with cell division. Mustard gas burns, like X-rays burns, heal only with difficulty, and even after they appear to have healed they have a tendency to break down again. In addition, it was found that vaginal epithelium of an ovariectomized mouse which has been exposed to a weak solution of mustard gas fails to manifest the mitotic activity which normally follows stimulation with estrogens, and that this inhibition of mitosis lasts for several weeks after the exposure to mustard gas. It is well known that the chromosome breaks and rearrangements caused by X-radiation interfere with cell proliferation, partly through mechanical disturbances of mitosis and partly through death of those cells which, after distribution of the fragments and new chromosome

combinations into the daughter cells, do not receive a sufficiently normal set of chromosomes. It was thought possible that mustard gas, like X-rays, may inhibit cell division through direct action on the chromosomes.

In the autumn of 1940, experiments were started to find out whether mustard gas is capable of producing gene mutations and chromosome rearrangements. *Drosophila melanogaster* was used as test animal. The flies were exposed to mustard gas vapor, first in a closed chamber and later in a container through which air mixed with mustard gas was sucked. The first results immediately gave promise of success. Both males and females became sterilized to a degree which depended on the dose. Sterility was found to be due to two independent causes, both of which are also known to be involved in the production of X-ray sterility. First, gametogenesis is inhibited, so that after a time no more ova and spermatozoa are available. Second, lethality is high among zygotes from treated eggs and, more important still, among eggs laid by untreated females which have been mated to treated males. Since the spermatozoa do not lose their motility as a result of the treatment, the most likely explanation was that mustard gas, like X-rays, produces chromosome breaks and rearrangements in the sperm.

In order to obtain conclusive proof that mustard gas exerts an action on the chromosomes, genetic methods for the detection of mutations were applied. Male flies were mated to untreated females, and the progeny (F_2) was examined for the occurrence of mutations. Early mutation work, as well as some more recent work on organisms which are genetically less thoroughly known than *Drosophila*, has suffered from the impossibility of eliminating the large personal error, for a trained worker may spot abnormalities which may pass unnoticed by a less experienced or less observant person. In *Drosophila* genetics this obstacle has been removed by methods which, in the main, have been designed by H. J. Muller, and without which the quantitative analysis of genetic radiation effects would have been impossible. The essential feature of these methods is their restriction to the detection of so-called lethal mutations, *i.e* mutations which are so harmful that they prevent development of the individual. Hence, lethal mutations are detected by the absence from the progeny of a whole class of flies, and since presence or absence are characteristics about which any two observers are likely to agree, these methods reduce the personal error to a minimum, while at the same time allowing the study of large samples without excessive labor. Particularly useful for large-scale tests are methods like the famous *ClB* test which are designed to detect sex-linked lethals, *i.e.* lethals on the sex chromosome, of which the male has only one, while the female has two. A sex-linked lethal prevents the development of a male carrying it, while it usually does not interfere seriously with development of the female. In the *ClB* test each treated or control sex-chromosome becomes subsequently represented, in the F_2, by a whole culture of flies, and if a lethal has arisen on a sex-chromosome, the corresponding culture will consist entirely of females—a fact which is, of course, readily observed even by an untrained person.

The result of the first *ClB* test with mustard gas, carried out in April 1941, was spectacular beyond expectation. Whereas the rate at which sex-linked lethals arise spontaneously in laboratory stocks rarely approaches 1 per cent, 90 lethals were found in about 1,300 treated sex-chromosomes. This represents a mutation rate of over 7 per cent. Only 3 sex-linked lethals were found in an equivalent number of untreated chromosomes, representing a rate of 0.2 per cent. Similar results had previously been obtained only with X-rays or other high-energy radiation. Further tests fully confirmed and even exceeded the first success, up to 24 per cent lethals being produced. Higher percentages can hardly be expected because, concomitantly with the increase in mutation rate, sterility becomes more and more severe.

Genetic analysis of the lethals produced in the first *ClB* test indicated that some of them were due to, or combined with, chromosome rearrangements, and these findings were confirmed by cytological examination carried out by Dr. Slizynski. A special test for the production of chromosome rearrangements by mustard gas was undertaken in December 1941. The method was designed to spot translocations, *i.e* rearrangements through which two chromosomes have exchanged portions with one another. Spontaneous translocations are so exceedingly rare that the use of controls was not considered necessary. The result left no doubt about the capacity of mustard gas to produce chromosome rearrangements; 7 translocations were found in 816 treated nuclei. A report on these results was sent to the Ministry of Supply in March 1942, but, like all this work, could not be published because of the security ban on work with war gases. In subsequent experiments more translocations as well as other types of rearrangements were produced. Since only *Drosophila* had been used for all these studies, it was gratifying that cytological investigations on pollen mother cells of *Tradescantia*, carried out by Dr. Koller in 1943, fully confirmed our finding that mustard gas can produce chromosome breaks and rearrangements.

The similarity between the genetic effects of mustard gas and of X-rays are so striking that only gradually did certain differences between the two types of action come to light. Yet special interest attaches just to these differences, because a comparison between chemical and physical mutagens seems a hopeful approach to the problem of mutation. The first difference appeared in work on translocations. It has been shown that the frequencies of X-ray-induced lethals, on the one hand, and of X-ray-induced translocations, on the other, bear a mathematical relationship to the dose administered,

the first increasing directly as the dose, the second approximately as its 3/2th power (*10*). Consequently, for a given dose of X-rays (as measured in roentgen units) there exists a numerical relationship between the numbers of lethals and translocations produced. Thus, a dose of 3,000 r-units produces about 9 per cent sex-linked lethals and about 6 per cent translocations between chromosomes II and III of *D. melanogaster*. After mustard gas treatment, this relationship is shifted very markedly in favor of sex-linked lethals. Instead of the expected 6 per cent, only 0.5 per cent translocations between chromosomes II and III were produced in an experiment in which the rate of sex-linked lethals was 9 per cent, and a similar relative shortage of translocations was observed in subsequent tests. At first sight, these observations seem to indicate that mustard gas is less efficient than X-rays in breaking the chromosome thread. However, it is well to be cautious in drawing this conclusion. It has to be kept in mind that with the methods used we could not detect the primary breaks, but only a proportion of the subsequently formed rearrangements. It is conceivable that chemical treatment interferes with the process of rejoining of broken ends in such a way that a given number of breaks results in fewer observable rearrangements than would be formed by the same number of X-ray breaks. Special tests are required to decide this point.

On the other hand, mustard gas does not seem to be less efficient than X-rays in the production of very small, so-called "minute" rearrangements. Slizynski and Slizynska (*17*), in a cytological of sex-linked lethals produced by various agencies, have found that in about 20 per cent of cases the genetic change underlying the production of a lethal is a minute deficiency in the chromosome, and this frequency appears to be the same after X-rays, after ultraviolet radiation, and after mustard gas treatment. These findings emphasize the similarity, often pointed out by geneticists, between true gene mutations and minute chromosome rearrangements, and they do not contradict the possibility that so-called gene mutations may be nothing more than chromosome rearrangements of so minute a size that they elude detection by cytological methods. It will be of great interest to determine whether small deficiencies form an equally high proportion of lethals which have been produced by less potent chemical substances than mustard gas.

A second difference between the actions of X-rays and of mustard gas came to light in the course of a study of visible mutations after chemical treatment. In one respect this study was disappointing since the mutations observed were of the same types as those found after X-ray treatment, and there was no indication of any specific effects of the gas on individual genes. Mustard gas seems to act as indiscriminately as X-radiation. There is, however, a difference between these two agencies which involves not the types of mutation which they produce, but the way in which the mutations become manifest in the offspring of the treated flies. After X-ray treatment of males most of the mutated offspring show the induced abnormality (such as yellow body color instead of the normal gray) over the whole surface of their body. Only a small proportion (less than 15 per cent) of the mutated individuals are mosaics, *i.e.* show the abnormality in a part of their body, the remainder being normal. In the progeny of mustard-gas-treated males, on the other hand, mosaics form a high proportion (usually between 30 and 50 per cent) of all mutated individuals (*2*). Moreover, whereas the gonads of X-ray mosaics rarely contain both normal and mutated cells, those of mustard gas mosaics quite frequently appear to do so. A special study has been made of such "gonadic mosaicism" with respect to sex-linked lethal mutations (*3*). A female, daughter of a treated male, whose ovaries contain a patch of tissue in which the cells carry a sex-linked lethal, will have fewer sons than a normal female, the shortage of sons depending on the relative sizes of the normal and mutated portions of the ovary. A similar depression of the sex ratio occurs also in the progeny of females who carry, evenly distributed through all cells of their ovaries, a sex-linked "semilethal" mutation, *i.e.* a mutation which weakens the males so that only a proportion of them are capable of completing development. Analysis of females giving a low sex ratio has shown that among daughters of irradiated males this abnormality is almost always due to a semilethal mutation affecting the whole of the ovary. On the other hand, in 9 out of 20 daughters of mustard-gas-treated males, the shortage of sons was due to the presence in their otherwise normal ovaries of a mosaic patch carrying a sex-linked lethal. Finally, mention should also be made of a striking case of mosaicism in which a son of a mustard-gas-treated male was, both in the gonads and in the soma, a mosiac for two different mutations of the same gene, although it must be assumed that in the treated spermatozoon each treated gene was present only once.

An explanation which seems particularly satisfactory in accounting for all these observations is that the gene affected by treatment does not always mutate at once, but may acquire a tendency to mutate which remains latent until a later cell division. Support for this hypothesis was obtained when it was found in several cases that the offspring of gonadic mosaics for a mutation again were gonadic mosaics for the same mutation. In these cases an induced specific instability seems to have been transmitted from one generation to the next before giving rise to a stable change. No parallel observations have been reported in literature on radiation genetics; but it seems worth noting that so-called "unstable" genes, *i.e.* genes which tend to mutate repeatedly in the same direction, have been found several times in untreated material (*6*).

The difference between the mutations produced by short-wave radiation and chemical reaction may be tentatively ascribed to the different amounts of energy involved in the two types of reaction. In short-wave radiation the energy made available is usually sufficiently large to produce a catastrophic alteration in the structure of the gene, by transforming it from one stable configuration to another. On the other hand, reaction of the gene with a chemical substance, because of the smaller amount of energy involved, may produce a less drastic effect, by transforming it to an intermediate metastable configuration. Such a configuration will, of course, tend to undergo "spontaneous"alteration to another and more stable configuration, *i.e.* an "unstable" gene is produced.

After the first positive results with mustard gas had been obtained, the search for chemical mutagens was extended to substances which either in their chemical structure or in their pharmacological action are related to mustard gas. Mustard gas is a fixative of protoplasm with unusual power of penetration. It was soon seen that these two properties by themselves are not sufficient to make a substance mutagenic, for neither osmic acid nor picric acid affected the mutation rate in tests in which the majority of the treated individuals were killed. Neither can it be said that every potent vesicant is a mutagen, for lewisite gave entirely negative results in two *ClB* tests. So far only three substances have been found which give genetic effects similar to those of mustard gas. These all belong to the class of nitrogen- or sulphur-mustards. Their chemical formulas are: (1) $O(CH_2 \cdot CH_2 \cdot S \cdot CH_2 \cdot CH_2Cl)_2$, (2) $N(CH_2 \cdot CH_2Cl)_3$, and (3) $CH_3 \cdot N(CH_2 \cdot CH_2Cl)_2$.

As the chemical mutagens presumably attack the genic material directly, it was noted with interest that these active compounds all contain an unsaturated atom (:S or ⋮N) which might combine with materials composing the gene, and that this activity would be enhanced by the type of side chains present in the vesicant mustards (e.g. $ClCH_2 \cdot CH_2$-). With this type of structure is associated the tendency to intramolecular cyclization to form onium compounds (*7*), characteristic of the active ⋮N and :S vesicants. Assuming that the mutagenic action is due to the reaction on the unsaturated atom of the uncyclized compound with the gene, it was thought likely that replacement of the :S and ⋮N by :O would not produce active materials, as the addition compounds of divalent oxygen are not stable in aqueous solution (and "O mustard" is not a vesicant). Stable addition compounds are, however, formed by compounds having the :CO group, and though the corresponding "CO mustards" were not tried, the tear gases, chloracetone and dichloracetone (compounds with $ClCH_2$- side chains instead of the $ClCH_2 \cdot CH_2$- of mustard gas) were examined. The activity of these compounds was extremely weak; in fact, the results were not clearly positive, although they suggest the possibility that both these compounds are slightly mutagenic. By analogy with the vesicant action of the :S compounds, the chlorethylacetones might be more active. It has not yet been possible to test these substances.

Other groups which might replace the :S and ⋮N of the mustards and retain the additive ability of the molecule include ⋮As, although compounds with ⋮As are rather unstable under physiological conditions and are mostly toxic. The corresponding ⋮P compounds are apparently out of the question in this connection, as they are spontaneously inflammable in air. The $:SO_2$ compounds may similarly be expected to show some activity, but not the :SO ones. This parallels their vesicant action. There is also the possibility of using nitrile, isonitrile, and the corresponding thiocyanates and isothiocyanates for the coordinating group, and attention was therefore directed to allyl isothiocyanate. A weak but definite mutagenic activity could be demonstrated for this compound (*4*).

On the other hand, this type of chemical structure does not seem a necessary prerequisite for a mutagenic substance. This is shown by the fact that Hadorn and Niggli (*8*) have obtained considerable numbers of mutations by exposing explanted ovaries of *Drosophila* to weak solutions of phenol.

Allyl isothiocyanate, or mustard oil, occurs naturally in plants of the genus *Brassica*. We do not know whether it acts as a mutagen in these plants, but it is interesting to speculate how far naturally occurring mutagens may be responsible for spontaneous mutability. It has been shown by Muller and Mott-Smith (*14*) that cosmic radiation and natural radioactivity are quantitatively insufficient to account for the observed rates of spontaneous mutation. Timoféeff-Ressovsky, Zimmer, and Delbrück (*20*) have suggested that random temperature oscillations inside the nucleus may occasionally overstep the energy threshold required for the production of a mutation. In the light of the results reported here it seems possible, however, that a certain proportion of natural mutations may be due to the action of mutagenic substances within the organism, and whose production may itself be the consequence of gene action. Such an assumption finds support in the known cases in which definite genes influence mutability of the rest of the genes or even of a specific gene (*2*, *11*, *17*). Search for natural mutagens is therefore of high interest, but may well turn out to be exceedingly difficult. By its very nature a natural mutagen can have no drastic effect in the species in which it occurs; otherwise, the species could not survive. Moreover, a physiological system which includes mutagens whose production is controlled by genes will, in the course of its evolution, have attained a finely attuned equilibrium between the strength of the effective substances and the sensitivity of the gene or genes on which they act. Removed from its normal genotypical environment, a natural mutagen may produce quite different effects or none at all. Therefore, results

btained with one organism may not be transferable to nother, in contrast to results gained with such drastic gencies as X-rays and, presumably, mustard gas. Nevertheless, it is tempting to consider the possibility hat one of the means by which evolution adapts mutbility to environmental requirements is the achievement of a balance between the production of mutagens nd sensitivity to them.

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Obituary

Henry Helm Clayton

1861–1946

With the passing of Henry Helm Clayton, on October 6, 1946, there ended a life of exceptional activity and eminence in meteorology, public service, and business.

Clayton was born on March 12, 1861, at Murfreesboro, Tennessee. Because of delicate health, early education was acquired in private schools and by study at home. It was during this period that his interest in meteorology developed.

Studies of local storms, beginning in 1878, were followed in 1882 by his first activity, aid in the organization of the newly formed Tennessee Weather Service, including analyses of reports and a gift of 30 rain gauges. In 1884–85 he was assistant at the Observatory of the University of Michigan and associate editor of the *American Meteorological Journal*. In February 1886, after three months at Harvard College Observatory, he joined the staff of Blue Hill Meteorological Observatory, founded by Abbott Lawrence Rotch in the preceding year, where he remained as assistant and meteorologist until 1909. During this period many important advances were initiated by him with the enthusiastic approval of Director Rotch. At first there was no assistant, and at various times, at his own expense, Clayton employed others to share his rapidly expanding program of research.

Clayton's studies of clouds, begun in 1886, yielded the first definite information concerning the circulation of the atmosphere over America and established the Clayton-Egnell law of the increase of velocity with height. The detailed observations during the period 1886–90 are the only hourly data of changes in form, height, and movement of clouds in the Western Hemisphere, and, with Clayton's discussion, undoubtedly stimulated the organization of the International Cloud Committee and the international series of measurements of heights and velocities of 1896. The colored pictures for the *Atlas of clouds*, issued in 1897 by the U. S. Hydrographic Office, were painted under Clayton's supervision. He was also consultant in the preparation of the first *International atlas* (1905).

Clayton's invitation to William A. Eddy to try his meteorological kites at Blue Hill led to the first use of kites to lift recording instruments, August 4, 1894, and to the adoption throughout the world of this method of sounding the atmosphere. Important results of Clayton's analyses of the accurate data obtained included the discovery of persistent, sharply defined stratifications in the lower atmosphere, and previously unsuspected, variable effects of mountains upon the surrounding atmosphere. Interest in this new method of research, later to be named "aerology," is indicated by his generosity in allowing free use in aerology, without royalty, of the form of Hargrave kite patented by him, which came into use at all aeronautical laboratories. Always envisaging improved techniques and advances in aerology, he encouraged Blue Hill to develop the first radio sonde, in 1935.

He described the solar eclipse as "a kind of laboratory experiment in which are eliminated practically all influences upon the atmosphere except that of a fall of temperature," and original studies led to his suggestion of the eclipse cyclone caused by the cooling of the air by the shadow.

Clayton's great interest in forecasting was first indicated by his paper, "A lately-discovered meteorological cycle," published in the *American Meteorological Journal* in August 1884. Later, at Blue Hill, his proof that forecasts made locally are better than those issued at a

distant central office caused the authorization of local forecasting at principal stations of the government weather service. An important public service at this time was his strongly supported effort toward removal of the national weather service to a civilian department, followed by action by Congress in 1891. He was local forecast official in the new Bureau, 1891–93, and in the *Blue Hill Weather Bulletin* of 1896–97, he published weekly forecasts based upon cycles. In 1910 he was invited to Argentina, where he was chief of the Forecast Service for nine years. There he inaugurated forecasting based upon variations in solar energy. On his return to the United States, Clayton continued this work in cooperation with the Smithsonian Institution and, starting a private weather service, forecasted and acted as consultant for business organizations while prosecuting his researches. At the beginning of World War II, the Government suspended private forecasting, but, during 1943–44, at the request of the Weather Bureau, he continued research on an extended scale to determine the relations between short-period changes of solar energy and variations of weather. This work, done through Harvard University, was aided by a statistical group maintained by the Weather Bureau.

Clayton's many studies of solar relations in cooperation with the Smithsonian Institution led to *World weather records*, a notable contribution to meteorology and climatology published by the Institution and highly praised by the International Meteorological Organization; the third volume is now in press. His researches were summarized in *World weather* (Macmillan, 1923) and in *Solar relations to weather* (Clayton Weather Service, 1943). A monograph amplifying earlier studies of the possible effects of the planets on solar variations, and of cycles, especially in their biological relationships, was completed only a month before his death.

In 1905 he headed the deBort-Rotch expedition for exploring the atmosphere over the Atlantic Ocean with kites and balloons. With Director Rotch, he represented Blue Hill at the International Meteorological Conference at Munich in 1891, and was delegate from Argentina to the first Pan-American Scientific Congress at Washington in 1915 and the Sixth International Meteorological Conference at Utrecht in 1923. In 1943 he was awarded a gold medal by the Foundation for the Study of Cycles. He was a charter member of the American Meteorological Society.

Clayton possessed the unusual combination of a vivid imagination, an ability to visualize atmospheric phenomena in their three dimensions, exceptional industry, steadfastness of purpose, and a keen sense of values. Throughout his life he was a pioneer, with all the courage and energy necessary to open new paths in spite of difficulties and hard knocks. Yet he was unassuming, warm and gracious in his manner, and always ready to concede values in points of view differing from his own.

STERLING P. FERGUSSON and
CHARLES F. BROOKS

Blue Hill Meteorological Observatory,
Harvard University

Officers of the AAAS, 1947

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NEWS
and Notes

Edmund E. Day, president of Cornell University and chairman of the Inter-Society Committee on Science Legislation created at the instigation of AAAS, appeared by invitation before the Interstate and Foreign Commerce Committee of the House of Representatives on March 6. The other members of the Executive Committee of the new group—Harlow Shapley, vice-chairman; Dael Wolfle, secretary-treasurer; R. G. Gustavson, chancellor, University of Nebraska; Ralph W. Gerard, University of Chicago; and Douglas M. Whitaker, Stanford University—also attended the hearings after holding the first meeting of the Executive Committee on March 5.

In presenting the opinion of the Inter-Society Committee, Chairman Day said in part:

... We need a National Science Foundation to help provide facilities and to help train scientific workers to use them.

There is no thought that a National Science Foundation will interfere with the excellent work being done by the private foundations and institutions, or the government agencies that are now active in research.

The private foundations, for a long time the major source of support for basic research and scholarships, welcome the relief provided their inadequate resources and have gone on record saying so.

The private colleges and universities as Dr. Conant, among others, has said, see no spectre of government control in accepting money for research and scholarships (*Science*, January 3). The research agencies in the government see the new Foundation as supplementing their restricted efforts. . . .

These views led to the introduction into the 79th Congress of two Science Foundation bills in the House of Representatives, H.R. 6448 by Representative Mills and H.R. 6672 by Representative Celler. Several bills were introduced into the Senate which were eventually combined in S. 1850, the Senate counterpart of the Celler bill. The Senate passed this bill (*Science*, May 10, 1946).

In July 1946 the House Committee on Interstate and Foreign Commerce considered the two bills, but in view of the many honest differences of opinion over details of these bills, wisely decided to defer action in order to allow fuller discussion of so important a matter in the 80th Congress (*Science*, July 26 and August 2, 1946).

That action allowed scientists themselves, and members of Congress, an opportunity to discuss and to consider the characteristics of a bill which will create the most effective National Science Foundation. The Inter-Society Committee of scientists, which I represent, was formed for the purpose of ascertaining, coordinating, and reporting the attitudes of American scientists toward the various issues involved in the creation of a National Science Foundation. The Committee held its first meeting in Washington on February 23.

There was complete unanimity at that meeting on the very great importance of establishing a National Science Foundation. The large attendance, the wide range of scientific societies represented, and the high competence of the scientists who attended were impressive proof of the importance given to securing effective action on the problem. . . .

The issue before this Committee is so important that we urge more extended study and further consideration of these bills. We expect to prepare a more definitive statement which will represent the best judgment of scientific opinion. We would like an opportunity to present it before this Committee at a later time.

About People

Harlow B. Mills, professor and head, Department of Zoology and Entomology, Montana State College, has been appointed chief, Illinois State Natural History Survey, to succeed the late Theodore H. Frison. Dr. Mills will assume his duties March 1.

Charles William Huntley, dean of Adelbert College, Western Reserve University, Cleveland, Ohio, became dean of Union College, Schenectady, New York, February 1, succeeding Charles F. F. Garis, who retired after 44 years at the college. Dr. Huntley, a psychologist, was a former student of Dr. Garis.

Lewis Hanford Tiffany, William Deering professor of botany and chairman, Department of Botany, Northwestern University, has been appointed to the Illinois State Board of Natural Resources and Conservation to succeed E. J. Kraus, University of Chicago.

Harold Schlosberg, Department of Psychology, Brown University, has been promoted to the rank of full professor. Prof. Schlosberg, who this past year has set up laboratory facilities for a new Distribution course in psychology, during the war wrote the monthly "Psychology News Letter" for distribution to foreign scientists by the Office of War Information.

William A. Hamor, Mellon Institute of Industrial Research, University of Pittsburgh, received the honorary LL.D. degree at the commencement of the University of Miami, Coral Gables, Florida, January 30.

Freeman S. Howlett has been made professor and acting chairman of the Department of Horticulture and Forestry, Ohio State University, Columbus, Ohio.

Chester Peterson, former director of the Inspection Division, Philadelphia Signal Corps Procurement District, has been appointed physicist in the Resistance Measurements Section, National Bureau of Standards. He will work with other members of the Bureau Staff on completion of an Absolute Measurement of Resistance, investigation of which was interrupted by the war.

Byron T. Shaw has been appointed assistant administrator of agricultural research, U. S. Department of Agriculture, to succeed W. V. Lambert, who became administrator last October. Dr. Shaw, a soils physicist, has been in charge of research in this subject in the Bureau of Plant Industry, Soils, and Agricultural Engineering since 1943. His new appointment begins March 10.

J. McDunnough, recently retired chief of the Systematic Unit, Division of Entomology, Canadian Department of Agriculture, has accepted a research associateship at the American Museum of Natural History, New York City, where he will continue studies on North American Lepidoptera.

Robert E. Campbell, Lt., Chemical Corps, has been made chief meteorologist for the Test Division, Technical Command, Edgewood Arsenal, Maryland.

F. L. Wynd, formerly of the University of Illinois, has been appointed professor of plant physiology and biochemistry at Michigan State College, East Lansing, and head of the Department of Botany and Plant Pathology to succeed E. A. Bessey.

George M. Stanley, associate professor of geology, University of Michigan, has been granted a sabbatical leave of absence for the university year 1947–48 to conduct research on the shorelines of extinct Pleistocene Lake Lahonton in western Nevada to determine recent crustal movements among the mountain ranges and intermontane basins occupied by various arms of this former large body of water. A similar study may be undertaken around Yellowstone Lake.

Paul S. Nicholes, formerly with the U. S. Biological Warfare Division, Camp Detrick, Maryland, has been named assistant professor of bacteriology, University of Utah School of Medicine, Salt Lake City, to replace W. E. Clapper, who recently accepted a position at the University of Colorado School of Medicine.

Visitors to U. S.

Australian scientists visiting this country include: S. M. Sykes, research officer, Division of Horticulture, New South Wales Department of Agriculture, who will attend the convention of the National Association of Frozen Food Packers to be held in San Francisco and will remain in this country about six months to study fruit and vegetable freezing; D. R. Ziedler, senior research officer, Division of Industrial Chemistry, Australian Council for Scientific and Industrial Research, who is spending several months at the Chemical Engineering Department, Massachusetts Institute of Technology; N. A. Esserman, chief, Division of Metrology, National Standards Laboratory, Sydney, Australia; and Ian Langlands, officer in charge of the Building Materials Research Division, Australian Council for Scientific and Industrial Research, who expects to remain in the United States for two months.

All of the above may be contacted through the British Commonwealth Scientific Office, Room 505, 1785 Massachusetts Avenue, N. W., Washington 6, D. C. (Attention: Mrs. V. Connell.)

B. Wasserstein, senior mineralogist, Geological Survey of the Union of South Africa, on study-leave in the United States, is taking courses at Massachusetts Institute of Technology, Cambridge, Massachusetts.

Kathleen Lonsdale, Royal Institution and University College, London, is conducting research at the National Institute of Health, Bethesda, Maryland, under a special research fellowship until the end of July. Dr. Lonsdale, one of the first two women elected to Fellowship of the Royal Society, will be at the California Institute of Technology during March. She is available to lecture on her work in X-ray crystallography while in this country.

Grants and Awards

The 11th Oberly Memorial Award, given by the University of South Carolina every two years for the outstanding bibliography in the field of agriculture or related sciences, will be made in the spring of 1947. Persons interested in competing for the prize should send four copies of their bibliography to W. P. Kellam, Chairman, Oberly Award Committee, University of South Carolina, Columbia.

The University of Illinois has accepted a grant of $6,400 a year for five to six years from the Herman Frasch Foundation, New York City, for investigating possibilities of increasing organic matter of soils under practical crop conditions and determining the role of organic matter in production of exceptionally high yields of corn and other crops.

Investigation will be conducted in the Soil Fertility Division, Department of Agronomy, under Roger H. Bray, Ernest E. DeTurk, and O. H. Sears.

Lyla Tupper Bradin is recipient of a $1,200 Ciba grant-in-aid to the Department of Biology, Johns Hopkins University, and the Department of Embryology, Carnegie Institution of Washington. The grant is to aid in a study of fetal maturity at birth as related to the maternal uterine environment before birth, with special reference to sensitivity of the respiratory center to anoxia and respiratory stimulant drugs.

The University of Texas Medical Branch, Galveston, has received an initial grant of $500 from J. B. Nail and alumni associates of Wichita Falls, Texas, for establishment of a research fund for the study of deafness. Dr. Nail indicated that the alumni of the Wichita Falls area will maintain this research fund by annual grants.

Western Reserve University has been granted $112,000 by the National Foundation for Infantile Paralysis to finance a five-year study of the effect of the polio virus on nerve and brain tissue. The following members of the Department of Biochemistry, School of Medicine, will participate: Harland G. Wood, head of the Department; Merton F. Utter, associate professor; John A. Muntz and Thomas P. Singer, assistant professors, and G. Robert Greenberg, instructor. These men will work with mice and cotton rats which have been infected by the Lansing strain of the polio virus.

Colleges and Universities

The University of Michigan has appointed Robert Travers, chief examiner, and Clyde Coombs, research psychologist, in the Bureau of Psychological Services, Institute for Human Adjustment, effective February 1.

The Utah State Agricultural College, Logan, Utah, has appointed E. L. Waldee, associate professor of plant pathology, and R. K. Gerber, assistant professor of horticulture. Dr. Waldee was on the staff of Iowa State College before entering the service, and Mr. Gerber had done government research in plant pathology.

The Department of Botany and Plant Pathology, Michigan State College, East Lansing, announces the following recent appointments: C. J. Alexopoulos, formerly deputy director of UNRRA in Greece, associate professor of mycology; W. B. Drew, University of Missouri, associate professor of ecology and taxonomy; G. W. Prescott, Albion College, associate professor of morphology and phycology; G. P. Steinbauer, University of Maine, associate professor of physiology and biochemistry; L. C.

orr, Cornell University, assistant fessor of plant pathology; R. Lowry, iversity of Michigan, assistant pro- sor of cytology and genetics; P. W. nnis, Independence Junior College, istant professor of botany; and J. liott, Coldwater, Michigan, High hool, instructor of botany.

mmer Programs

The Mount Desert Island Biological boratory, Salsbury Cove, Maine, is ugurating a new summer laboratory study of problems in aseptic cultiva- and nutrition of organisms and sues. The laboratory, for independent vestigators and advanced students, will nder Philip R. White, general physi- gist, Institute for Cancer Research, iladelphia.

Some of the problems now visualized in vitro cultivation of invertebrate vertebrate tissues; meristematic tis- s of algae, mosses, ferns, and sper- tophytes; excised embryos of ferns, sses, marine algae, and flowering nts; embryonic stages of invertebrate imals such as the brine shrimp and of nivorous invertebrates such as hy- oids; and slime molds. Questions of trition, and control and manipulation morphogenesis will have an important ce in the studies.

The fee will be $100 for the season tending from June 15 to September 15 for any part of the season. Applica- ns should be sent to Philip R. White stitute for Cancer Research, Girard and rinthian Avenues, Philadelphia 30, fore March 15.

eetings

The Centennial Celebration of the w York Academy of Medicine was augurated March 6 with a dinner at e Waldorf-Astoria Hotel at which John Ryle, professor of social medicine, ford University, England, gave the incipal address, "Social Pathology and e New Era in Medicine." William Dwyer, mayor of the city of New York, d George Baehr, president of the Acad- y, also spoke.

Throughout the celebration a series meetings and conferences will be held sections of the Academy and affi- ted organizations, and a number of exhibitions will be placed on view. The following five Institutes will also be held: Library Methods and Problems, March 11–12; Social Medicine, March 19–21; Public Health, April 1–3; Medical Education, April 16–18; and Hospitals, April 21–23.

All meetings except the first day of the New York Academy of Sciences Conference, March 21, will be held at the Academy of Medicine Building, 2 East 103rd Street, New York. Exhibits will be at the Academy building, Metropolitan Museum of Art, New York Historical Society, Museum of the City of New York, and the New York Public Library.

Elections

The California Academy of Sciences has elected the following men as Fellows in recognition of distinction in scientific work: L. H. Brown, G. F. Ferris, J. W. MacBain, and C. B. van Niel, Stanford University; F. A. Jenkins, Harold Kirby, and E. G. Linsley, University of California, Berkeley; Peter Frendsen, University of Nevada; H. U. Sverdrup, director, Scripps Institution of Oceanography; and S. B. Show, who recently resigned as regional forester of the Forest Service, San Francisco, to accept a post with UNESCO.

The American Astronomical Society has elected the following foreign astronomers to honorary membership in the Society: Megh Nad Saha, University of Calcutta, India; Gavriil A. Tikhov, U.S.S.R.; Bertil Lindblad, Stockholm Observatory, Saltsjobaden, Sweden; Jan H. Oort, Sterrewacht, Leiden, Netherlands; E. A. Milne, Oxford, England; and Bernard Lyot, Observatoire de Meudon, France.

Recent Deaths

Sir John Flett, 77, director of the Geological Survey of Great Britain and the Museum of Practical Geology between 1920 and 1935, died January 26.

Kurt Lewin, 56, director of the Research Center of Group Dynamics, Department of Economics and Social Sciences, Massachusetts Institute of Technology, died February 12 at Cambridge, Massachusetts. He was formerly professor of child psychology at the Child Welfare Research Station, University of Iowa, Iowa City.

Walter Ivan Lillie, 55, head of the Department of Ophthalmology, Temple University Medical School, died February 21 in Philadelphia.

Henry Beaumont, professor of psychology and director of the Bureau of Industrial Psychology, University of Kentucky, died at his home in Lexington February 21.

Horace A. Shonle, 55, director, Organic Chemistry Division, Eli Lilly and Company, died February 24 after a brief illness from pneumonia.

NRC News

A grant of $10,000 has been received from the Viking Fund to aid anthropological research in the Pacific area under the Pacific Science Board of the NRC. The Board, in cooperation with the Council's Pacific Committee on the Anthropological Sciences and the Navy Department, is engaged in developing plans for a coordinated program of anthropological and associated research in Micronesia. The Council has also received a grant of $5,000 from the Coolidge Foundation for the general fund of the Pacific Science Board.

Make Plans for—

Crystallographic Society, 2nd annual meeting, March 19–21, U. S. Naval Academy, Annapolis, Maryland.

Western Metal Congress and Exposition, fifth, March 22–27, Civic Auditoriums, Oakland, California.

World Health Organization Interim Commission, March 31, Geneva, Switzerland.

Midwest Power Conference, March 31–April 2, Palmer House, Chicago.

American Association of Anatomists, annual meeting, April 3–5, Mount Royal Hotel, Montreal, Canada.

Institute of Mathematical Statistics, meeting on stochastic processes and noise, April 24–25, New York City.

National Academy of Sciences, annual meeting, April 28–30, Academy Building, Washington, D. C.

COMMENTS

by Readers

Researchers can extend their work and reduce the burden of calculation if they use punch cards and tabulating machines.

As Neil R. Bartlett suggests (*Science*, October 18, 1946), many scientific workers are unfamiliar with punch-card techniques. His plan for multiplying in order to obtain the sum of X,X^2, XY,Y^2, we have used to multiply 8 four-digit numbers and summary punch the totals all at one time. These summary cards, which carry the progressive totals for the digit used as multiplier, may then be added into the grand total, which is summary punched, and thus the product sums desired are obtained without the manual work he describes.

The card method is especially valuable whenever there are many variables in the matrix to be multiplied and where the N is large.

We have expanded the use of cards into factor-analysis calculations. The centroid method has been described (D. M. Hall, E. L. Walker, and Isabelle Crawford. *Psychometrika*, June 1945), and we are now perfecting the principal factor method procedures. (D. M. HALL, *University of Illinois.*)

Chronic vitamin B_1 deprivation in litters of dogs can affect social dominance as measured by biting without retaliation, the order in which animals go to the food pan, and the relative or absolute immunity from attack by other animals in the group. There have been a number of studies demonstrating the existence of social dominance among such vertebrates as hens, mice, canaries, cattle, and dogs; and changes in dominance have been studied in connection with hormone administration, as testosterone propionate, restriction of cage space, and with social variables, as introducing a new animal into an established social group (W. C. Allee. *Biol. Symp.*, 1942, **8**, 139–162).

It was found in connection with another study in 1941 (I. A. Berg. *J. exp. Psychol.*, 1944, **34**, 343–368) that social hierarchies existed in each of five litters of puppies. In one litter of four males and one female, the least dominant animal, a male, was so severely bitten and so regularly driven from the feeding pan that he was isolated in a separate cage and given a special diet which included milk and raw beef. The other animals had earlier been placed on an exclusive diet of water, canned dog food, and a type of dry dog chow. After three weeks the isolated animal was again placed in the cage with his littermates with the result that he reversed his previous social position and became the dominant animal of the litter after several fights with each of his littermates.

About a week after this an increasing loss of appetite, followed by symptoms of "Fright Disease," was noted in those animals which had been fed for several months on the commercial dog food ration. Following the suggestion made by J. W. Patton (*Vet. Med.*, 1939, **34**, 372–381), 600 I.U. thiamine chloride were injected subcutaneously in all five animals daily for four days. Patton had noted that commercial dog foods are usually autoclaved and that B_1, being heat labile, is destroyed as a result of the autoclaving.

It is believed that the chronic B_1 deficiency resulting from the autoclaved dog food was directly related to observed changes in social dominance in this litter; for, after the series of B_1 injections, a number of fights ensued, and the previously dominant male resumed his ascendant position in the social hierarchy. The male which had originally been lowest and, after the special diet, highest in dominance ended as third highest in the social group of littermates. The female was lowest in the new hierarchy. This final order of dominance remained for almost two months, when no further observations were made. Similar dominance shifts associated with B_1 deprivation were noted in other litters.

It is suggested that investigators of social dominance and of hormonal effects on behavior take special precautions to ensure an adequate B_1 supply in the animals' diet, since, in addition to the effects noted here on dominance, testicular hypofunction or atrophy (C. H. Best and N. B. Taylor. *Physiological basis of medical practice.* 3rd ed., 1943. p. 1297) accompanied by reduced sex hormone secretion, can result from B_1 deficiency. (IRWIN AUGUST BERG, *University of Illinois.*)

C. Perrier and E. Segrè (*J. Chem. Phys.*, 1937, **5**; 1938, **6**) showed that radioactive isotopes of element 43 could be formed by neutron or deuteron bombardment of molybdenum. Several chemical properties of element 43 were established at the time, as well as some nuclear properties of the spectral isotopes. These isotopes were found in nuclear bombardments by the 37-inch cyclotron of the Radiation Laboratory, University of California.

Later, C. S. Wu and E. Segrè (*Phys. Rev.*, 1940, **57**) found element 43 among the fission products of uranium, a source from which relatively large amounts of 43 can be isolated.

It seems appropriate now to give this element the name technetium, from the Greek τεχνητός, artificial, in recognition of the fact that technetium is the first artificially made element. The corresponding chemical symbol should be Tc.

In 1940 D. R. Corson, K. R. Mackenzie, and E. Segrè (*Phys. Rev.*, 1940, **57**) prepared the isotope of mass 211 of element 85 by bombarding bismuth with alpha particles accelerated in the 60-inch cyclotron of the Radiation Laboratory, University of California. At that time they established several chemical properties of element 85 and made a rather complete nuclear study of the isotope formed.

A name should now be given to this new element and, following the system by which the lighter halogens chlorine, bromine, and iodine have been named—by modifying a Greek adjective denoting some property of the substance in question—the discoverers propose to call element 85 astatine, from the Greek ἄστατος, unstable. Astatine is, in fact, the only halogen without stable isotopes. The corresponding chemical symbol proposed is At. (E. SEGRÈ, *University of California, Berkeley.*)

Comparison of the Provisions of S. 525 and S. 526

S. 525	S. 526
Compromise bill, S. 1850, as passed by the Senate, July 3, 1946	A new measure, similar to the original Magnuson Bill, S. 1285
ORGANIZATION	
Board	*Foundation*
A National Science Board of 9 members is to be appointed by the President, by and with the advice and consent of the Senate, plus the chairmen of the several divisional scientific committees (originally 7).	The Foundation is to have 48 members appointed by the President, by and with the advice and consent of the Senate. The President is requested to give due consideration to recommendations from the National Academy of Sciences or other scientific or educational organizations.
Term of office is to be 3 years with possibility of reappointment after a lapse of 1 year.	Term of office is to be 8 years, with possibility of reappointment after a lapse of 4 years.
The Board is required to meet 6 times a year.	The Foundation is required to meet once a year or at the call of its chairman.
(In this bill the Foundation is defined as a government agency including the Board, all advisory and employed personnel.)	
Divisional Structure	*Divisional Structure*
The Foundation is to contain Divisions of: Mathematical and Physical Sciences; Biological Sciences; Health and Medical Sciences; National Defense; Engineering and Technology; Scientific Personnel and Education; Publications and Information.	The Foundation is to contain a Division of National Defense which is to report to the Foundation. Until otherwise provided by the Foundation, there shall also be Divisions of: Medical Research; Mathematical, Physical, and Engineering Sciences; Biological Sciences; Scientific Personnel and Education for the granting of all scholarships. The Foundation is empowered to enlarge the number of Divisions as necessary.
The functions of the Divisions are to be prescribed by the Administrator on the advice of the Board.	
ADMINISTRATION	
Board	*Executive Committee*
The Board is to appoint its own executive secretary whose salary is not to exceed $12,000 annually.	The Foundation is to elect biennially from its own members an Executive Committee of 9.
The Board is to elect a chairman annually from its own membership.	The Executive Committee is to choose its own chairman and vice-chairman biennially; ex-officio principal officers of the Foundation.
	The Executive Committee is required to meet 6 times a year.
	The Executive Committee is to establish advisory committees as it sees fit.
The President is to appoint an Administrator, by and with the advice of the Senate, after receiving recommendations from the Board; compensation is to be $15,000 annually.	The Executive Committee is to appoint a Director, with the approval of a majority of the Foundation, whose salary is to be $15,000 and who is to report to the Executive Committee.
	The Executive Committee is required to make an annual report to the President and Congress, making appropriate recommendations.
Administrator	*Director*
The Administrator is to appoint a Deputy at $12,000 annual compensation.	The Director may appoint a Deputy whose annual compensation must not exceed $12,000.
The Administrator is to appoint the Directors of various divisions, who are to be full-time employees at $12,000 a year.	The Director is to appoint and fix compensation of other personnel.
The Administrator is to appoint other personnel as he deems necessary and at rates he determines.	
The Administrator is required to consult with the Board and through the Directors with the divisional committees in exercising his authority.	
The Administrator is to establish advisory committees as he sees fit.	

Divisional Committees

The Division of National Defense is to be a committee of not more than 40, at least half civilians, appointed by the Administrator, the remainder divided equally between appointees of the Secretaries of War and Navy.

The Executive Committee for the Division of National Defense is to consist of 5 members: the chairman of the divisional committee, 2 civilians, and 2 officers designated by the Army and Navy, respectively. The civilians are to be elected annually by the civilian members of the divisional committee.

Each Division except National Defense is to consist of a scientific committee of not less than 5 or more than 15 members, appointed by the Administrator with the advice and approval of the Board.

The members of the divisional committees are to serve 3-year terms.

Each divisional committee is to elect its own chairman from among its own members.

Each divisional committee is required to meet at least 6 times a year.

The Division of National Defense is to be a committee, appointed by the Foundation, of not less than 8 or more than 40. One half are to be civilians, appointed by the Foundation; the remainder, representatives designated in equal numbers by the Secretaries of War and Navy.

The Executive Committee for the Division of National Defense is to consist of 5 members: the chairman of the divisional committee, 2 civilians, and 2 designated by the Army and Navy, respectively. The civilians are to be elected annually by the civilian members of the divisional committee.

Each Division except National Defense is to consist of a scientific committee of not less than 5 members appointed by the Foundation.

The term of each member is to be fixed by the appointing authority.

Each divisional committee is to elect its own chairman from among its own members.

Expenditure of Funds

Of the available funds, a minimum of 15 per cent is to be allocated to National Defense, and a minimum of 15 per cent to the Division of Health and Medical Sciences.

A minimum of 25 per cent of all funds (exclusive of those for National Defense) is to be distributed on a geographic and population basis among the states. These amounts are to be expended only for research and development activities in tax-supported colleges and universities, including land-grant colleges.

An additional amount of not less than 25 per cent may be expended in nonprofit organizations.

Activities of the Foundation shall only supplement those of other government agencies authorized to do scientific research and development.

No specific provision is made for the distribution of research funds allotted to the Foundation.

Appointment of Personnel

The Administrator is to have the authority to waive the usual civil-service regulations covering employees.

The Director is to have the authority to waive the usual civil-service regulations covering employees.

The Deputy Director is specifically exempt from civil-service rules.

Publication

Provision is made for full dissemination of scientific and technical information consistent with national security.

Provision is made for full dissemination of scientific and technical information consistent with national security.

Scientific Personnel and Scholarships

The Administrator is to maintain a register of scientific and technical personnel and to provide in general a central clearing-house for information concerning such personnel.

The National Roster is to be transferred to the Foundation.

Fellowships and scholarships are provided for in any field of science in institutions of the candidates' own choosing in the United States and abroad.

The Foundation is to maintain a register of scientific and technical personnel and to provide in general a central clearing-house for information concerning such personnel.

The National Roster is not specifically mentioned.

Scholarships and graduate fellowships are provided for in all fields of science in institutions of the candidates' own choosing in the United States and abroad.

Research Findings and Patent Rights

A series of specific standards are provided which will govern the Administrator in the disposition of inventions and findings. (Identical with S. 1850.)

The Foundation is to have complete authority to dispose of inventions "in a manner calculated to protect the public interest and equities" of the contracting parties.

TECHNICAL PAPERS

Effect of Urethane on Mouse Myelogenous Leukemia[1]

RUBY M. ENGSTROM, ARTHUR KIRSCHBAUM, and HARRY W. MIXER[2]

Departments of Anatomy and *Radiology, University of Minnesota Medical School*

It has been reported that the administration of urethane to human leukemic patients produces an effect similar to that following treatment with X-rays (*2*). In preliminary experiments the authors have investigated the effects of urethane on normal and leukemic myeloid tissues of mice.

The leukemia used in this investigation was a transplanted myelogenous chloroleukemia in the fifth transfer generation. The disease developed was a chronic leukemia with the white blood-cell count always rising to more than 100,000 cells/mm.[3] This transfer line was derived from a spontaneous leukemia which had arisen in an F_1 hybrid mouse between strains F (high leukemia) and NH (low leukemia), transfer has always been into mice of this hybrid genetic constitution. The disease developed in 76 of 77 mice inoculated, and there were no spontaneous recoveries. Six to eight weeks after inoculation, white blood-cell counts were decidedly elevated, and the spleen was palpable. Mice survived as long as four months following the intraperitoneal inoculation of leukemic cells suspended in isotonic saline. The blood picture was typical of myelogenous leukemia, with stem cells and all intermediate forms down to mature leucocytes. Anemia developed as the disease progressed to fatal termination.

Urethane[3] in aqueous solution was administered intraperitoneally, the daily dose ranging from 0.004 to 1.0 mg./gram of body weight. The dose per gram of mouse was contained in 0.01 cc. of distilled water. After three daily doses of either 0.5 or 1.0 mg./gram of body weight (the latter is an anesthetic dose), white blood-cell counts dropped from over 100,000 cells/mm.[3] to normal levels, the only mononuclear cells of the circulating blood being lymphocytes. Spleen and lymph nodes were definitely reduced in size, although microscopic examination revealed that these organs, the lung, and liver contained leukemic cells. The cellular picture of the bone marrow was altered. In contrast to the decided left shift in white cell development characterizing the marrow of mice with myeloid leukemia, many mature leucocytes were now present. A similar alteration was noted after X-ray therapy (three to five daily doses of 80 r to the whole body), with the counts also dropping to normal levels. Reduction in size of spleen and lymph nodes was greater, however, following urethane treatment. The effect of urethane was similar in all of 13 mice treated with this dose. This transplanted leukemia failed to respond in a similar manner to either Fowler's solution, benzol, or colchicine.

Within three days after daily treatments with urethane in doses of either 0.5 or 1.0 mg./gram of body weight, leukemic mice lost as much as 7 grams (initial weight, 25–28 grams). When the daily dose of urethane was reduced to 0.2 mg./gram of body weight, leucocyte counts still dropped, but weight loss was not appreciable. Counts fell from 150,000–200,000 to 50,000 white blood cells within 7 days, but the lymph nodes and spleen were not decreased in size. This dose of urethane proved ineffective in maintaining the low leucocyte counts previously induced by larger doses. Although the white blood-cell counts rose, and spleen and lymph nodes increased in size, the percentage of mature leucocytes in the blood was greater than that seen in untreated animals. Larger doses of urethane again brought down the white counts and reduced the size of spleen and lymph nodes.

A single dose of 0.1 mg. of urethane/gram of body weight effected a significant dip in the white count in the first 24 hours, followed by a prompt rise to the initial level. There was no further response to the daily administration of this small dose. Doses of less than 0.1 mg. did not alter the white counts.

Experiments are being undertaken to determine whether life can be prolonged when leukemic mice of this transfer line are treated with urethane. In future experiments treatment will also be started earlier in the development of the transplanted disease. Mouse leukemia should provide favorable material with which to determine under controlled conditions the possible effect of urethane on survival time in the human disease.

Two cases of spontaneous mouse leukemia have also been treated with urethane. One, a lymphatic leukemia with a white blood-cell count of 63,000, failed to respond to daily injections of 0.2 mg./gram of body weight. The second, a myelogenous leukemia, responded in the same manner as the transplanted disease, exhibiting a depression in leucocyte count from 82,000 to 20,000 within a week, and decrease in size of the spleen.

It is of interest that in these experiments the response of mouse leukemia to urethane was comparable to that seen in human leukemia (*2*). Urethane has been shown to retard the growth of certain neoplasms of the mouse and human, although the alteration was not permanent (*1*). In the present experiments it was noted that if treatment with urethane was discontinued, the white blood-cell counts became elevated, and spleen and lymph nodes enlarged. In two instances, however, the counts remained depressed for almost two weeks after cessation of treatment. Two weeks is a relatively long time in the course of mouse leukemia.

Urethane induced a depression in the leucocyte count of nonleukemic human subjects (*2*). In normal mice doses of 0.5 or 1.0 mg./gram of body weight produced a similar effect, but neither the drop in leucocyte count nor loss of body weight

[1] This investigation has been aided by grants from the Jane Coffin Childs Memorial Fund for Medical Research, the National Cancer Institute, and the Cancer Fund of the Graduate School of the University of Minnesota.

[2] National Cancer Institute Trainee in Radiology.

[3] Urethane Merck (ethyl urethane-ethyl carbamate).

appeared as rapidly as in leukemic mice similarly treated. Daily doses of 0.2 mg. or less/gram of body weight given for three weeks proved to be nontoxic for normal mice. Doses of urethane which affected leukemic marrows produced no striking cytologic alterations in the bone marrow of normal mice.

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The Role of Arsenic in the Production of Alcoholic Polyneuritis

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In view of the experimental work which led to the discovery of BAL (British anti-lewisite) it might be worth while to mention some unpublished results obtained on the urinary excretion of arsenic in patients suffering from alcoholic polyneuritis. The signs and symptoms of arsenic polyneuritis are so similar to those seen in alcoholic polyneuritis that it seemed possible that arsenic as well as alcohol with its concomitant avitaminosis played a role in the latter. Twenty-four patients on the wards and 5 from the Outpatient Department of the Boston City Hospital were studied for urinary arsenic excretion. Fourteen of these suffered from alcoholic polyneuritis, while 15 patients were utilized as a control group.

Six of the 14 patients had paralysis and loss of sensation of all four extremities; 5 had a moderate, and 3 a mild, type of polyneuritis. (The additional diagnosis of Korsakoff's psychosis was made in 5, delirium tremens in 1, and signs of pellagra were present in 2.)

The 15 patients utilized as a control group fell into four groups: (1) those suffering from acute infective polyneuritis; (2) patients suffering from chronic alcoholism without signs of neuritis; (3) a group chosen at random on the ward; and (4) some outpatients who had had alcoholic polyneuritis in the past but who denied the use of alcohol at the time tested.

An attempt was made to collect at least three 24-hour urine specimens from the 24 hospitalized patients. Several had more than 3 specimens tested; the maximum was 11. Only one or more single specimens were collected from the 5 outpatients. The Reinsch test was used on all specimens, and those from 2 patients containing the largest amounts of arsenic were checked by the Gutzeit quantitative test. One patient was excreting as much as .227 mg. of arsenic/1,000 cc. of urine.

The more severe the paralysis, the more positive were these tests for arsenic. Arsenic is not a normal constituent of the body but is present due to ingestion with food. It is possible that alcohol affects the storage of arsenic, which in turn contributes to the interference with enzyme action already present in these malnourished patients.

The 14 patients suffering from alcoholic polyneuritis were consistently excreting significant amounts of arsenic in the urine, while the 15 in the control group showed only an occasional trace of this element.

Mass Mortality of Marine Animals on the Lower West Coast of Florida, November 1946–January 1947

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Catastrophic mass death involving millions of fish recently occurred on the south Florida Gulf Coast. In the latter part of November 1946, mackerel fishermen noted dead and dying fish and turtles in streaks of discolored water 10–14 miles offshore from Naples. The mortality moved northward and reached Boca Grande by January 10. Fish continued dying in the bays behind Captiva and Sanibel Islands as late as January 29. Investigations carried out since January 15 have resulted in the following observations.

Dead fish, in association with discolored water, were reported from Dry Tortugas to Boca Grande, a distance of 130 miles. At Fort Myers on January 19 the beach was littered with fish in excess of 170/foot of shore line, in addition to those floating on the water in bays and sounds and to a distance of 10 miles offshore. One homeowner on Captiva Island reported burying 60,000 fish from 200 feet of bay beach. The same area had to be cleaned on three other occasions. The total number of dead fish over the whole area was estimated to be over 50,000,000. Oysters, clams, crabs, shrimp, barnacles, and coquinas were also killed. The clam industry at Marco, 50 miles south of Fort Myers, and the sponge industry north of Tampa Bay do not appear to have been involved, nor, in spite of an isolated report of dead fish from a vessel passing Dry Tortugas, does the mortality appear to have reached the Florida Keys. All kinds of fish succumbed. Mackerel seemed to be relatively unaffected, but many mullet were killed. Floating carcasses of black drum, tarpon, groupers, and large jewfish were the most spectacular sights.

Reports of the phenomenon were not received by the writers until the middle of January. From January 18 onward, the water was sampled chemically and with plankton nets near Sanibel Island, where dying fish were encountered; at Fort Myers Beach, where dead fish only were found; and at Naples, where the water was beginning to clear up and the fishermen were making mackerel catches.

Reddish-brown discoloration of the water was observed off Fort Myers Beach. Plankton examination showed this to be unusually rich, consisting predominantly of copepods and invertebrate larvae with little phytoplankton. At Clam Bay dying fish were seen in streaks of greenish-yellow water. These streaks contained large quantities of diatoms with *Coscinodiscus* sp. as the dominant organism, together with considerable detritus and smaller numbers of naked flagellates resembling species of *Gymnodinium*. The water at Naples, which was not discolored, contained copepods and a great abundance of *Rhizosolenia* sp. No one species was overwhelmingly predominant at all stations, but the organisms tentatively identified as *Gymnodinium* sp. were found in varying numbers in samples from the areas where fish were still dying.

[1] The writers are much indebted to J. N. Darling, of Captiva, Florida, for information and assistance given during the course of this investigation.

A patch of vivid yellow water, seen south of Useppa Island on January 28, consisted almost exclusively of *Gymnodinium* sp. with a mixture of numerous larval invertebrates. The water was viscid and slimy, having the consistency of diluted syrup. A fish was seen dying in this water.

Chemical determinations disclosed no unusual salinities. Water temperatures ranged from 22.5° C. to 26° C. Samples showed a pH close to 8.2. The dissolved oxygen content was not low in brownish-red water near Fort Myers Beach except in an inshore area where large numbers of dead fish littered the water. In the yellow patch of water described above the oxygen content was low, being less than 33 per cent saturated. Hydrogen sulfide was reported earlier at Naples, and the hulls of several fishing vessels were seen with the white topside paint definitely blackened. During the period of investigation no H_2S could be detected.

An odorless but acrid gas causing stinging of the nostrils and hard coughing made life miserable for the residents of Captiva Island when a northwest wind caused a heavy surf on the Gulf Beach from January 22 to 26. This gas, which could not be identified, was not present during calm weather on January 28, but could be detected by boiling samples of Gulf and bay water. It was particularly strong in a sample of the yellow water. Lund (*1*) has previously called attention to presence of this gas during a similar heavy mortality of fishes on the Texas Coast.

A report giving full details of observations on this phenomenon will be published later.

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The Glyceride Structure of Natural Fats

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Naturally occurring fats and oils consist predominantly of esters of glycerol and fatty acids, each hydroxyl group of the glycerol being esterified with a mole of fatty acid. A number of different fatty acids (usually at least four) make up any given fat. Because of the number of fatty acids and the fact that there are three positions on each glycerol molecule to which the fatty acids may be attached, a large number of isomeric glycerides is possible in a single natural fat. Thus, if n represents the number of component acids, the theoretical number of isomers possible from a maximum distribution of the acids over the three positions of glycerol is n^3. The actual number of glycerides chemically distinguishable from one another is $\frac{1}{2}(n^3 + n^2)$ (*4*).

In general, the glycerides of natural fats are highly mixed, simple triglycerides being the exception rather than the rule and occurring for the most part only in the relatively few fats in which a single fatty acid predominates. Since natural fats consist largely of isomeric glycerides, many of which differ from each other only slightly with respect to physical and chemical properties, the analysis of fats for their component glycerides has been an extremely difficult problem. For many years various investigators, especially Prof. Hilditch and his co-workers, have attempted to enlarge upon our rather meager knowledge of the glyceride structure of natural fats. The chief result of the investigations at the University of Liverpool has been the pronouncement of the so-called "rule of even distribution" (*3*). According to this hypothesis, the individual fatty acids of a fat tend to be apportioned evenly among the different glyceride molecules. In seed fats, for example, it is pointed out that trisaturated glycerides do not usually appear until the proportion of fatty acids reaches approximately 60 per cent. Numerous exceptions to this rule have been discussed by Hilditch, and a rough classification of fats has been made on the basis of their conformity to this rule.

An analysis of the "rule of even distribution," however, reveals the fact that truly "even" distribution is not proposed. Rather, it is maintained that, at fatty acid molar concentrations of approximately 60 per cent, homogeneous triglycerides of that fatty acid first appear—something less than "even" distribution. Frequently an association ratio (molar ratio of saturated to unsaturated fatty acids) of 1.4:1.0 is used, which is equivalent to a 58 per cent molar concentration of saturated fatty acids. On the basis of a truly "even" distribution, however, no homogeneous triglyceride should be formed until the molar concentration of the fatty acid in question is 66.7 per cent—that is, until more than two-thirds of the fatty acid molecules are the same. This is illustrated in Fig. 1, in which 10

Fig. 1

glyceride molecules are shown graphically. It is apparent that 20 saturated fatty acid radicals could be attached to the glycerol molecules without any glyceride containing more than two saturated fatty acids. The 21st saturated fatty acid, however, must unite with a glyceride already containing two molecules of the same fatty acid, consequently producing a molecule of trisaturated glyceride. An extension of this reasoning to a greater number of glycerol molecules leads to the obvious conclusion that only when the molar concentration of the saturated fatty acids exceeds two-thirds would saturated triglycerides be formed under a truly "even" distribution. Thus, the molar concentration of trisaturated glycerides, $[S_3]$, can be related to the molar concentration of saturated fatty acids, [S], as follows:

$$[S_3] = 3\,([S] - 66.7).$$

In general terms, if S_3 represents the triglycerides of any fatty acid, S, then the above equation defines "even" distribution as the term is employed in this paper.

Prof. Hilditch (*3*) has noted that fruit coat fats do not ad-

here well to the "even distribution hypothesis" and that land animal fats in general constitute notable exceptions. He has further pointed out that the glyceride structure of natural animal fats corresponds to that of synthetic mixed glycerides, in which the relationship of trisaturated glycerides, [S_3], to mole per cent saturated acids, [S], is expressed by the equation

$$[S_3] = k[S]^3,$$

where S_3 and S have the same significance as in the previous equation and k is a proportionality constant. Thus, the mole per cent of trisaturated glycerides is proportional to the cube of the mole per cent of saturated fatty acids. It should be noted that this equation is a specific example of the general equation $Y = k\ (X)^3$, which expresses the probability of any given arrangement of three independent variables. This, of course, is quite different from "even" distribution and, as will be shown later, really describes so-called "random" distribution.

In the chemical synthesis of glycerides from mixed fatty acids and glycerol, the amounts of the various glycerides

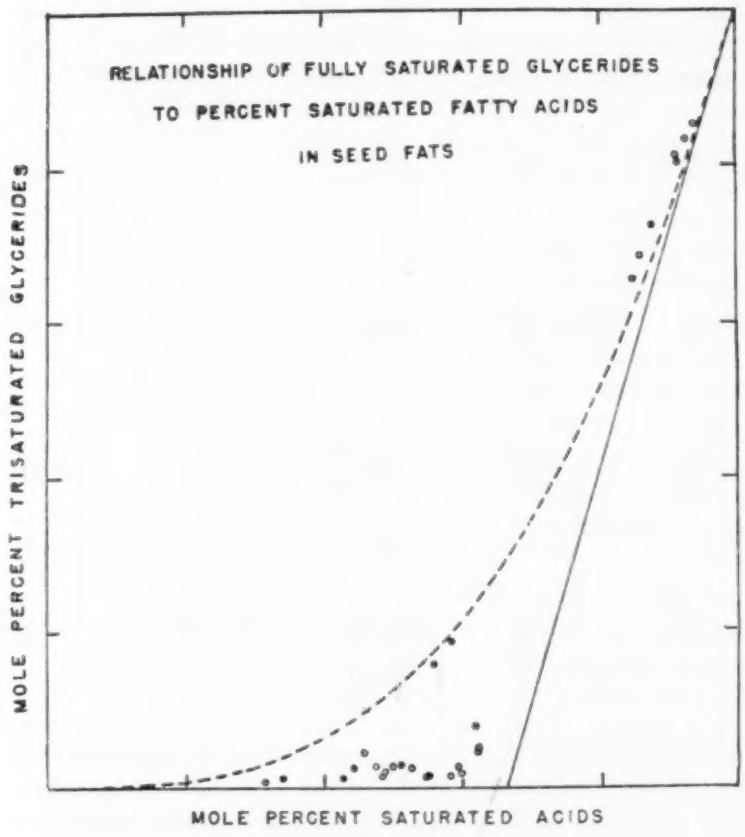

FIG. 2

formed would be expected to depend upon random collision and reaction, which is amenable to mathematical treatment on the basis of the laws of probability. Thus, the probability of oleic, palmitic, and stearic acids (equal reactivity assumed for each) uniting with glycerol depends upon their respective concentration; that is, the probability of oleo-palmito-stearin being formed is expressed by the equation:

$$[(OPS)] = k\ [O]\ [P]\ [S].$$

Increasing the concentration of any one of these acids increases the probability of that triglyceride being formed. It follows that if all the saturated acids were lumped together as S, the equation for the per cent of trisaturated glycerides would be:

$$[(SSS)] = k\ [S]\ [S]\ [S] = k\ [S]^3.$$

Experimentally, the only component of a glyceride mixture which can be determined with relative ease and accuracy is the trisaturated glyceride fraction. In the past it has been tacitly assumed that the total glyceride structure may be deduced if the relationship between saturated fatty acids and trisaturated glycerides is known. As a result, this relationship has been rather extensively investigated (*3*). In Figs. 2, 3, and 4 representative data from the literature are compared with curves representing the above equations for "even" and "random" distribution.

From Fig. 2 it is apparent that the experimental data for seed fats do not coincide well with either the straight line representing "even" distribution or with the curve representing "random" distribution. However, it must be noted that, according to Hilditch's hypothesis, the intercept of the straight line with the axis would be at approximately 58 mole per cent saturated acid rather than at 66.7 per cent, which represents truly "even" distribution. This transposition of the curve to the 58 per cent intercept would, of course, result in a better agreement of some of the points with the so-called "even distribution hypothesis." It should also be noted that the points in the upper part of the curve fit either "even" or "random" distribution about equally well. To illustrate this point, in Table 1 we have compared the amount of trisaturated glycerides anticipated on the bases of "even" and of "random" distribution in fats containing large amounts of saturated fatty acids. It is evident that, at high saturated fatty acid concentrations, calculations based upon the two theories give so nearly identical results that data obtained for fats in this range (85 per cent or more saturated acids) cannot be interpreted as favoring either hypothesis.

TABLE 1

MOLAR CONCENTRATIONS OF TRISATURATED GLYCERIDES CALCULATED FOR FATS CONTAINING HIGH MOLAR CONCENTRATIONS OF SATURATED ACIDS

Molar concentration of saturated acids	Molar concentration of trisaturated glyceride	
	Calculated for "even" distribution	Calculated for "random" distribution
94	81.9	83.0
93	78.9	80.3
92	75.9	77.8
91	72.9	75.3
90	69.9	72.9
85	54.9	61.3

In Fig. 3 the molar concentration of saturated acids versus that of trisaturated glycerides is plotted for fruit coat fats. In this case it is seen that the data definitely do not agree with those expected on the basis of either hypothesis.

Similar data for animal fats, as shown in Fig. 4, reveal that the molar concentrations of trisaturated glycerides in animal fats closely approximate the values anticipated from the equation $[Y] = k\ [X]^3$. From this observation it may be generalized that the over-all glyceride structures of animal fats probably approximate those which would be anticipated from a "random" distribution of the fatty acids over the available glycerol molecules. The same generalization has been proposed by Dean, who used the terms "indiscriminate" and "haphazard" to define the distribution of fatty acids in animal fats and synthetic glycerides (*2*). The term "random distribution" was

later used by Longenecker (*5*), who elaborated the general equation $[Y] = k\,[X]^3$ to include specific glycerides of all pos-

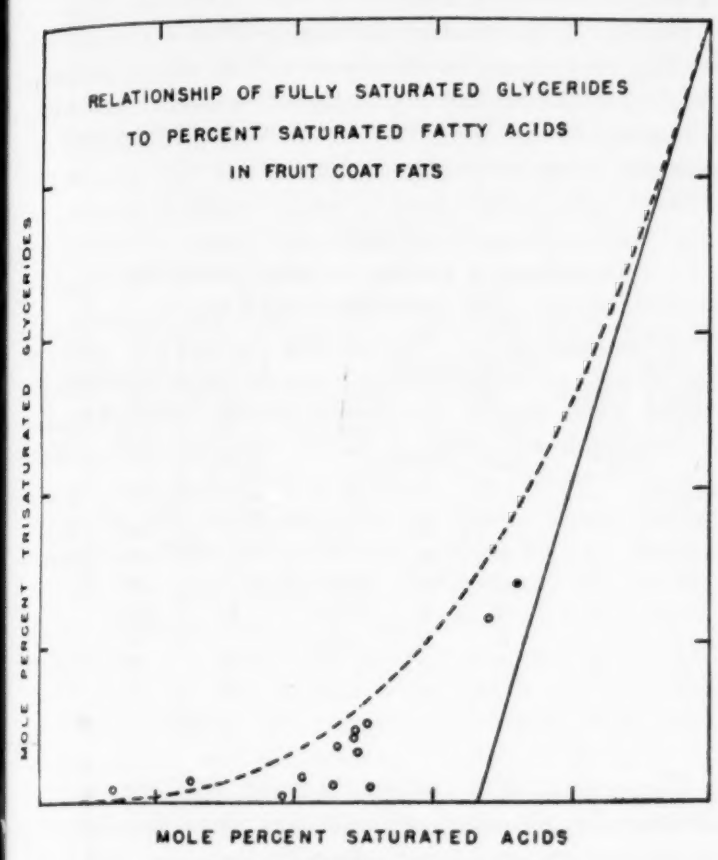

FIG. 3

sible configurations. Similar equations have recently been published by Bailey (*1*).

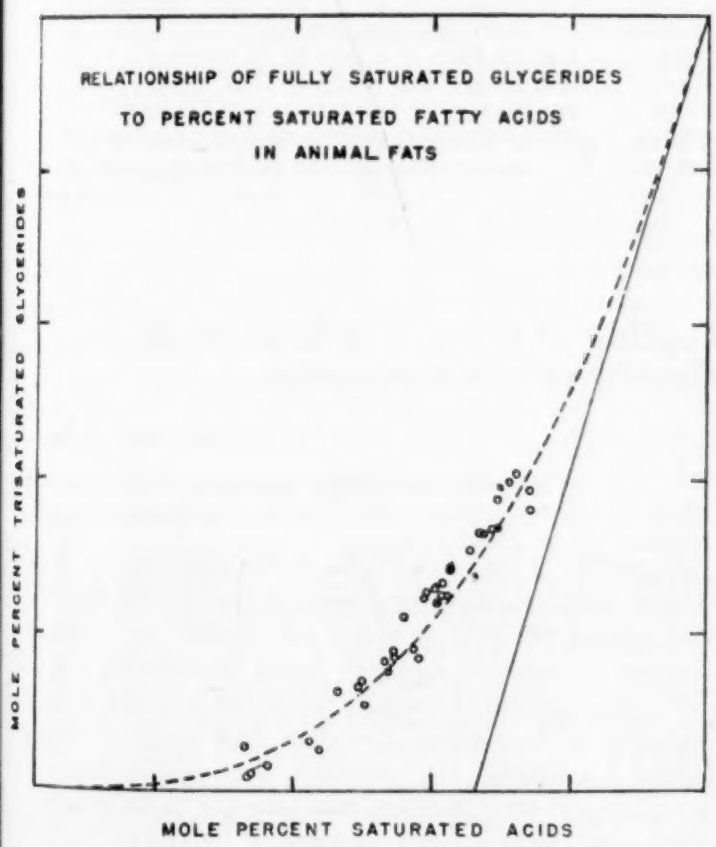

FIG. 4

In summary, an analysis of representative data showing the relationship of the molar concentrations of trisaturated glycerides to those of saturated acids in natural fats reveals that in the case of animal fats the glycerides are formed by a "random" or nearly "random" distribution of fatty acid radicals among the glycerol molecules. It has been shown that the "even distribution hypothesis" does not represent truly "even" distribution, but rather is an approach to the latter, being more or less arbitrarily fitted to experimental data. No general class of fats adheres to truly "even" distribution. Seed fats appear to approach the trisaturated glyceride contents anticipated by the "even distribution hypothesis," but even here the data are inconclusive.

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Effect of Vitamin B Complex on Inactivation of Estrone *in Vivo* and *in Vitro*

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In 1934 Zondek (*6*) found that estrone is inactivated by animals and plants. In experiments carried out *in vivo*, rats were injected with estrone and killed a few hours later. The bodies were finely minced, extracted, and the extract assayed as to estrogenic activity. Only about 2–4 per cent of the estrogenic activity of the injected estrone solution was recovered. Subsequent hydrolysis improved the recovery to 6–20 per cent. The major part of the inactivation was therefore not due to esterification. In numerous experiments inactivation of estrone by rats *in vivo* was consistently observed. Over a period of many years we have not chanced upon a single case in which such inactivation failed to occur.

In experiments carried out *in vitro*, pulps of various organs were incubated for some hours with estrone at 37°C., the mixture then being tested for estrogen activity. It was found that liver brei inactivates estrone to an extent of about 90 per cent, while of other organs tested only spleen inactivates estrone to a small degree. Hydrolysis of the inactive mixture does not liberate any estrogenic activity. It should be mentioned that not all livers tested inactivate estrone: for some unexplained reason, liver brei of normal rats occasionally fails to mediate this reaction.

Since heating inactivates liver pulp estrone, it may be concluded that the inactivation is enzymatic. This enzyme, which has been designated by one of us (B. Z.) as estrinase, has been obtained in cell-free extracts of liver and of various plants (*6*, *7*). The plant enzyme is closely associated with tyrosinase and inactivates estrone presumably by oxidation (*5*).

Recently Biskind and Biskind (*1*) have pointed to the existence of a relationship between the amount of vitamin B com-

[1] Aided by a grant from the Rockefeller Foundation.

plex in liver and the ability to inactivate estrone. These authors implanted pellets of estrone into spleens of adult castrated female rats. On a normal diet the animals remained anestrous. When the rats were given a vitamin B-complex-free diet, vaginal estrus occurred. In another series of experiments Biskind and Shelesnyak (*2*) castrated female rats and transplanted one ovary into the spleen. On a normal diet they remained anestrous, but when kept on vitamin B-complex-free diet, estrus appeared.

TABLE 1

INACTIVATION OF ESTRONE BY VITAMIN B-COMPLEX-DEFICIENT RATS *in Vivo*

Rat No.	Duration of vitamin B-complex-free diet (days)	Wt. of animal (grams)		Time elapsed between injection of estrone and killing of rat (hrs.)	Amount of estrone injected (I.U.)	Recovery of estrone (%)
		Start	Final			
1	33	25	23	5	2,000	0–10
2	30	25	20	5	1,600	10
3	30	25	25	5	2,000	10
4	30	40	32	4	1,000	10
5	30	45	36	4	1,000	10
6	30	42	35	4	1,000	25
7	30	40	27	4	1,000	0–10
8	30	40	29	4	1,000	0–10
9	32	47	35	2	2,000	25
10	32	47	37	2	2,000	50

Shipley and György (*3*) observed an impairment of ability to inactivate estrone *in vivo* in rats maintained on diets low in protein and high in fat. Vitamin B-complex deficiency induced similar but less constant response. Not all strains of rats tested by these authors reacted to the vitamin B-complex deficiency with less ability to inactivate estrone.

Singher, *et al.* (*4*) examined the dependence of inactivation of estrogens on vitamin B-complex deficiency and have shown that liver slices of riboflavin- and thiamine-deficient rats are unable to inactivate estradiol.

In experiments carried out on 28 vitamin B-complex-deficient female rats we have found that vitamin B deficiency has no influence on the inactivation of estrone by rats *in vivo*. Table 1 summarizes the results obtained with 10 rats kept for one month on a vitamin B-complex-free diet.[2] Most of the animals were near death after three weeks of the experiment, and a few died from cachexia caused by vitamin B-complex deficiency before the inactivation test could be performed. In the inactivation experiments, vitamin B-complex-deficient rats were injected with 1,000–2,000 I.U. of estrone.[3] These were killed 2–5 hours following the injection, and the minced bodies were analyzed as to their estrogenic content by the Allen-Doisy method. The inactivation after 2 hours was of the order of 50–70 per cent; after 4–5 hours, 75–100 per cent.

On the other hand, liver pulps of avitaminotic rats, contrary to normal liver, in a majority of cases uniformly fail to inactivate estrone. Table 2 shows results obtained with liver brei of 7 vitamin B-complex-deficient rats incubated with 250–500 I.U. of estrone in phosphate buffer pH 7.3 at 37°C. for 3–5 hours. The recovery of estrone was quantitative, and only in one case was there a measurable loss (25 per cent) of original estrogenic activity.

Hence, (1) the vitamin B-complex-deficient rats are able to inactivate estrone *in vivo* as are normal rats; (2) whereas the liver of normal rats inactivates estrone *in vitro* in a high percentage of cases, liver of vitamin B-complex-deficient rats does not inactivate estrone *in vitro*.

TABLE 2

INACTIVATION OF ESTRONE BY LIVER BREI OF VITAMIN B-COMPLEX-DEFICIENT RATS

Rat No.	Duration of vitamin B-complex-free diet (days)	Wt. of animals (grams)		Wt. of liver (grams)	Time of incubation with estrone at 37°C. (hrs.)	Amount of estrone used (I.U.)	Recovery of estrone (%)
		Start	Final				
11	25		40	1,600	5	500	100
12	22	40	30	1,700	4	500	100
13	22	40	32	1,650	4	500	100
14	35	45	40	1,800	4	500	100
15	28	45	36	1,550	3	500	75
16	28	48	37	1,700	3	500	100
17	23	45	24	1,800	3	250	100

The question as to whether the inability of liver of vitamin B-deficient rats to inactivate estrone *in vitro* is due to vitamin B-complex deficiency is under investigation.

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[2] We are obliged to Dr. M. L. Tainter, Winthrop Chemical Company, Rensselaer, New York, for supplying us with this material.

[3] We are indebted to Dr. B. J. Brent, Roche Organon, Inc., who supplied the estrone.

Feeding of Oysters in Relation to Density of Microorganisms

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Regardless of extensive studies on the physiology of oysters (*Ostrea virginica*), many problems concerned with their food and feeding are still unsolved and several are vigorously debated. For example, biologists do not agree on the effects of different quantities of material suspended in water upon the efficiency of the feeding of oysters. One group of workers, headed by Kellogg (*2*), maintains that oysters and other lamellibranchs are able to feed only when the water is comparatively clear, while another, represented by Grave (*1*), states that they can feed even in very turbid water. To clarify at least certain aspects of this problem we have made a study of the effect of different concentrations of microorganisms upon the rate of water pumping and, therefore, feeding of oysters.

Experiments in which oysters were fed *Chlorella* sp., *Nitzschia closterium*, *Euglena viridis*, other plankton forms, and a common variety of yeast have shown that there are rather definite concentrations above which the density of the microorganisms begins to interfere with the feeding of oysters. These concentrations corresponded to approximately 2,000,000 *Chlorella*, 70,000 *Nitzschia*, and 3,000 *Euglena*/cc. of water. As may be seen, the size of the cells played an important part because a much higher number of small cells, such as *Chlorella*, was needed to produce the same effect as that caused by a smaller number of larger organisms.

In concentrations higher than those given above, the rate of feeding was reduced, and the character of the shell movement of the oysters changed noticeably. In many experiments a correlation was noticed between the density of the microorganisms and the rate of feeding. When the plankton cells were too abundant, little or no food was swallowed by the oysters and the crystalline style was usually absent. Under such conditions the oysters ejected large quantities of pseudofeces to cleanse their gills and palps of an excessive accumulation of plankton. Sometimes the shells remained open for periods of several hours, although no water was pumped. If the oysters were kept in heavy concentrations for a long time, they became sluggish, their responses to stimuli diminished, and the tonus of the adductor muscle was partially lost.

Both the filtrate of the cultures, containing metabolic products of the cells, and the cells themselves affected the oysters because the rate of feeding was reduced or even entirely stopped when they were subjected to strong concentrations of either component.

When, after exposure to heavy concentrations of microorganisms, the oysters were again subjected to a flow of sea water, their rate of feeding usually showed a marked increase. The intensive pumping of water indicated an attempt to remove the microrganisms which had accumulated in the gills and mantle chamber.

In light concentrations, which contained fewer cells than those mentioned above, the rate of feeding and the shell movements remained normal. In many instances the rate of feeding was even greater than when the oysters were kept in running sea water. The possibility is not excluded that the presence of small quantities of plankton in sea water stimulates the pumping activities of the oysters.

The quantities of pseudofeces formed by the oysters were usually roughly proportional to the quantities of plankton present in the water, whereas a reverse relationship existed in the formation of true feces. The presence of large quantities of pseudofeces usually indicated that feeding proceeded under the relatively unfavorable conditions caused by heavy concentrations of plankton in the water. Small quantities of pseudofeces, or their absence, in the presence of large quantities of true feces showed that the oysters were feeding efficiently.

The results of our experiments indicate that both Kellogg and Grave were only partially correct in their conclusions. The opinion advanced by Kellogg, that oysters feed most efficiently only if the water contains small quantities of suspended matter, was corroborated by our studies. Contrary to his opinion, nevertheless, we found that oysters can also feed in water containing a relatively large number of microorganisms, although under such a condition the rate of feeding is decreased. It is true, however, that when the plankton is too heavy, the oysters cease feeding. On the other hand, Grave's conclusion may be considered correct only if it was qualified with the statement that the efficiency of feeding of oysters decreases in water rich in microorganisms. Since no such statement was made by Grave, his conclusion creates the impression that it is unimportant whether or not the water is relatively clear or heavily laden.

A full description of these studies will appear in the official publication of the U. S. Fish and Wildlife Service.

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Antagonistic Effect of *Corynebacterium diphtheriae gravis*

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The object of this note is to report the occurrence of an antibiotic effect produced by *Corynebacterium diphtheriae gravis* against several organisms. This strain of *C. diphtheriae gravis* was isolated in a culture from a diphtheritic throat and was identical in all particulars to the requirements of this organism. It was the specimen used in instruction of medical bacteriology at the Naval Medical School.

In checking its characteristics on potassium tellurite blood agar, the plate containing 15 mg. potassium tellurite/100 ml. blood agar became contaminated with *Bacillus subtilis*. The result is shown in Fig. 1. The black, clearly defined colonies are

Fig. 1

C. diphtheriae; the confluent growth, *B. subtilis*. About many of the *C. diphtheriae* colonies is a clearly defined zone where growth of *B. subtilis* has been inhibited.

Using moist blood agar plates containing the same amount of potassium tellurite, the strain of *C. diphtheriae gravis* was tested against *Proteus vulgaris*, *Salmonella typhimurium*, and *S. paratyphi A*. The same inhibitory effect was observed.

In October 1945 one of us was discharged from the Navy and this investigation ceased, although cultures of the organism were carried for future work. Eight months later an attempt was made to repeat and amplify the above experiments. During the extended period of storage and irregular transfer, however. the organism had apparently lost its ability to produce the inhibitory effect, and no antagonistic activity was demonstrable. Prior to loss of this effect no attempt was made to separate the diphtheritic exotoxin from the possible antibiotic substance.

Since there is no previous record of antagonistic activity of *C. diphtheriae*, this note is presented merely to record the fact that *C. diphtheriae gravis* may produce an antibiotic substance and to stimulate others to look for it among strains of this genus.

Mechanism of Sex Determination

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It has long been known that the ratio of males to females, 106:100 (*7*) in man, deviates appreciably from the 100:100 ratio which is predicted on the basis of the chromosome theory. This deviation has also been observed in plants and in other animals. Correns (*3*) thought that in plants, among other influences, might be the different masses of the male- and female-producing pollen grains. Bluhm (*2*), in her work with white mice, suggested the different masses of the two types of sperm as a factor, stating that male-producing sperms (androsperms) may have a better chance to reach the egg than the gynosperms because of their lesser mass of chromosome. Zeleny and Faust (*6*) found dimorphism in the sperm cells of 15 animal species. They believe that the two types of sperm are androsperms and gynosperms and that, due to their different masses, they may have different chances to reach the egg. Parkes (*5*) found dimorphism in the case of man, the rat, and the mouse.

This explanation involves the assumption that the average kinetic energy of both types of cell is the same, so that the two types travel with different velocities due to their differences in mass.

The purpose of this paper is to show that, to produce an appreciable difference between the velocities of the two types of cells, the differences in mass would have to be larger than could reasonably be expected.

By the definition of kinetic energy,

$$KE_x = \tfrac{1}{2}m_x v_x^2 \quad \text{and} \quad KE_y = \tfrac{1}{2}m_y v_y^2,$$

where KE_x is the average kinetic energy of a gynosperm; KE_y, that of an androsperm; m_x, the average mass of a gynosperm; and v_x, the average velocity of a gynosperm.

If the average kinetic energy of androsperms and gynosperms is equal,

$$\tfrac{1}{2}m_x v_x^2 = \tfrac{1}{2}m_y v_y^2.$$

Hence,

$$\frac{m_x}{m_y} = \left(\frac{v_y}{v_x}\right)^2.$$

Thus, the ratio of the masses of gynosperms to androsperms must be equal to the inverse ratio of the velocities of the two types of cells, squared. However, the number of males born must be proportional to v_y, and the number of females to v_x; hence, for a ratio of, for example, 106 males:100 females, we have:

$$\frac{v_y}{v_x} = \frac{106}{100} = 1.06. \quad \text{Since } \left(\frac{v_y}{v_x}\right)^2 = 1.1236, \frac{m_x}{m_y} = 1.1236.$$

This means that, to account for a ratio of 106:100, an average difference of about 12 per cent would have to exist between the masses of androsperms and gynosperms. If one takes into consideration the high index of mortality of male zygotes, the primary ratio of males to females must be at least 116:100 (*1*). Using this ratio in the above calculation, one obtains: $\frac{m_x}{m_y} = 1.3456$, which would be a difference of about 35 per cent in the average masses of androsperms and gynosperms.

The difference is mass is presumably due to that of only one chromosome (*4*). It then becomes apparent that the difference in mass between androsperms and gynosperms would have to be far greater than cytological evidence permits us to deduce in order to explain this great deviation from the normally expected 100:100 ratio, if mass of chromosome alone were to be considered the decisive factor.

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Effects of X-Radiation on Thymus Nucleic Acid

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Since the work of Muller in 1927, X-rays have become a tool in the production of chromosomal aberrations and artificial mutations in plant and animal cells. Although the effects of X-radiation have been investigated with regard to the organism as a whole and to its cellular and nuclear constituents, no clearly defined mechanism of action has emerged. The occurrence of nucleic acid, especially the desoxyribose type, in the chromosomes of all known cells warrants an investigation of the effects of X-rays on this substance.

Hollaender, Greenstein, and Jenrette (*3*) have shown that ultraviolet radiation produces a marked decrease in the structural viscosity and streaming birefringence of aqueous solutions of sodium thymus nucleate (TNA). Similarly, Sparrow (*4*) has demonstrated a fall in the viscosity of TNA upon X-radiation, the degree of change varying with the total dosage given. Since Sparrow's viscosity data were obtained at unknown velocity gradients, no conclusions can be reached regarding the structural viscosity of his solutions. In order to follow changes in structural viscosity it is necessary to measure the relative viscosity of the solution over a range of applied external pressures. When this is done, it is found that a marked decrease in structural viscosity occurs in TNA solutions irradiated with X-rays, similar to the change induced with ultraviolet radiation (see *2*), indicating an apparent decrease in the asymmetry of the nucleic acid particle with either type of irradiation.

Early in these studies it was noted that relative viscosity measurements at various pressures, made immediately at the end of the X-radiation period, cannot be compared because of the gradual decrease in the viscosity of TNA which occurs. This decay continues over a period of 18–24 hours, after which time the rate of fall in viscosity of the X-rayed sample approaches that of the control. Only then can comparative pressure studies be carried out. This continuous drop in viscosity subsequent to the cessation of X-radiation is shown in Fig. 1. The readings of relative viscosity taken 30 minutes after irradiation, allowing time for temperature equilibration, were: control, 22.9; 5-minute X-ray (28,000 r), 10.4; 10-minute X-ray (56,000 r), 7.3. The per cent of this first viscosity measurement is then plotted as a function of the time after irradiation.

Experiments were carried out on a dialysed solution of 0.7 per cent sodium thymus nucleate, prepared by the Hammarsten method from calf thymus. Viscosity was measured, relative to distilled water, in Bingham-Jackson viscometers at known pressures and at 30°C. X-ray dosage was delivered at the rate of 5,600 r-units/minute.

The rate of fall of the relative viscosity of TNA after the initial drop is markedly dependent upon temperature. If measurements of viscosity are carried out at 0°, the subsequent drop in viscosity with time is inhibited; both control and irradiated samples retain their viscosity as first measured. When brought up to 30°, after 5 hours at 0°, however, the per

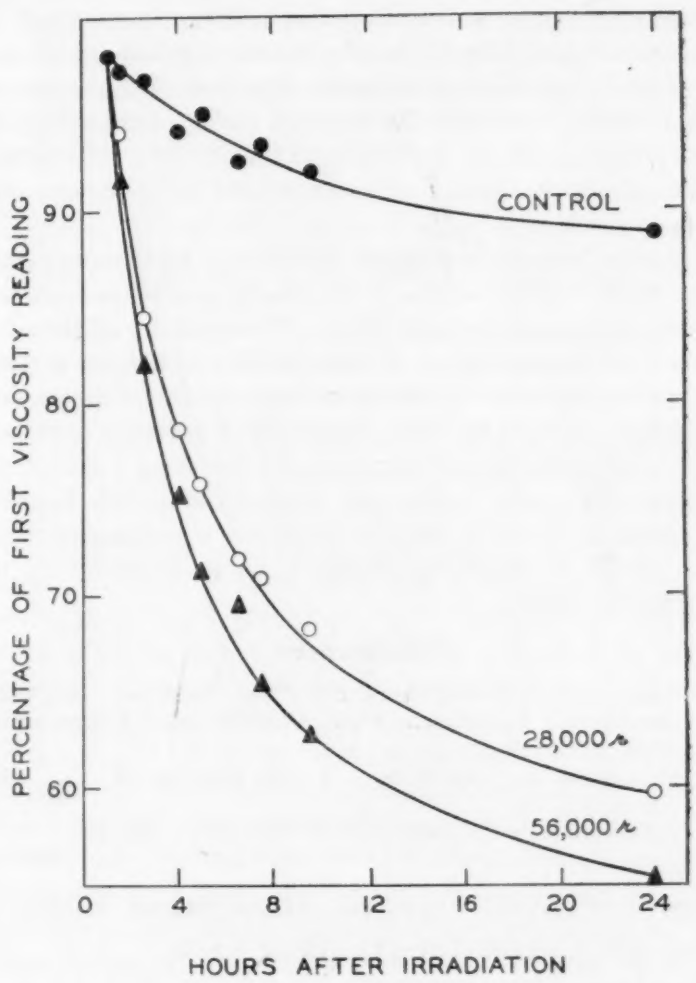

FIG. 1. Rate of decrease in viscosity of solutions of sodium thymus nucleate in terms of per cent of first reading at end of X-radiation period. Dialysed nucleate concentration was 0.7 per cent; temperature, 30°C.; external pressure, 18.4 cm. water.

cent drop in viscosity of the X-rayed sample is consistently greater than that of the control. Thus, at least two phenomena are observed: (1) the primary effect of X-rays to decrease the viscosity of TNA, which is proportional to the dosage, acts during the exposure to X-rays and is independent of the temperature; and (2) a secondary, progressive, presumably indirect effect is manifested only at the higher temperature of 30° and cannot be detected at 0°C.

It appears improbable that peroxide formed as a product of the X-radiation of water is concerned to any significant extent with the phenomena observed. Water was irradiated at 5,600 r/minute for 20 minutes and then added to a concentrated solution of nucleic acid. The drop in viscosity on standing was no different from that of a control diluted with the same

amount of untreated water. The addition of H_2O_2 to a solution of TNA in concentrations of 10^{-3} and 10^{-6}M caused neither an initial nor a continuous drop in viscosity. It appears likely that the secondary decay in the viscosity of the TNA is the result of progressive intramolecular alterations in the nucleic acid particle, which are set in motion by the primary effect of the X-radiation.

In order to ascertain the nature of the change brought about by X-radiation of TNA, a series of chemical and enzymatic studies were undertaken. These results indicate that there is no splitting off of ammonia or inorganic phosphate upon irradiation; neither are any titratable acid groups opened up. Spectroscopic studies on the dialysates of control and X-rayed samples, according to the technique described by Carter and Greenstein (*1*), show that there has been no splitting off of purine- or pyrimidine-containing fragments small enough to penetrate a cellophane membrane. Presumably this indicates that if depolymerization has occurred, the molecular weight of the product molecules is still greater than 10,000. The ultraviolet absorption spectra of the control and X-rayed nucleates are identical.

Purified desoxyribonuclease (McCarty's preparation) and rat tissue extracts behave in an exactly parallel fashion toward control and X-rayed TNA. The specificity of the substance, as determined by its susceptibility to enzyme action, is in no way altered by the irradiation. Whatever the way in which the particle has been changed by X-radiation (whether by depolymerization or rearrangement involving a change in shape), the change in the axial ratio of the particle has not involved a splitting of primary linkages or a rearrangement of the spatial configurations necessary for its susceptibility to enzymatic attack.

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An Improved Oxygen Absorption Bulb for the Carpenter-Haldane Gas Analysis Apparatus

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One of the most time-consuming aspects of basal metabolism determination by the open-circuit method of Lewis (*2*) is the Carpenter-Haldane process (*1*) of gas analysis. Though this method yields excellent results, it is most tedious and laborious, particularly the process of oxygen absorption by an alkaline pyrogallol solution. To insure complete absorption of oxygen, the analyst must pass the gas sample into the pyrogallol tube about 25 times while he watches a weird little windshield wiper "burp" a rubber bulb to facilitate automatic circulation of the pyrogallol solution from the reservoir.

Numerous efforts toward a more rapid absorption procedure proved that the old Hempel tube method was highly applicable. The Carpenter oxygen absorption tube was replaced by a simple bulb with a capillary stem arranged so that it could be easily shaken by hand, and the original 800-cc. pyrogallol reservoir was replaced by a small 200-cc. bulb fitted with a water seal. The windshield wiper circulator was found unnecessary when the small volume of solution was more frequently renewed.

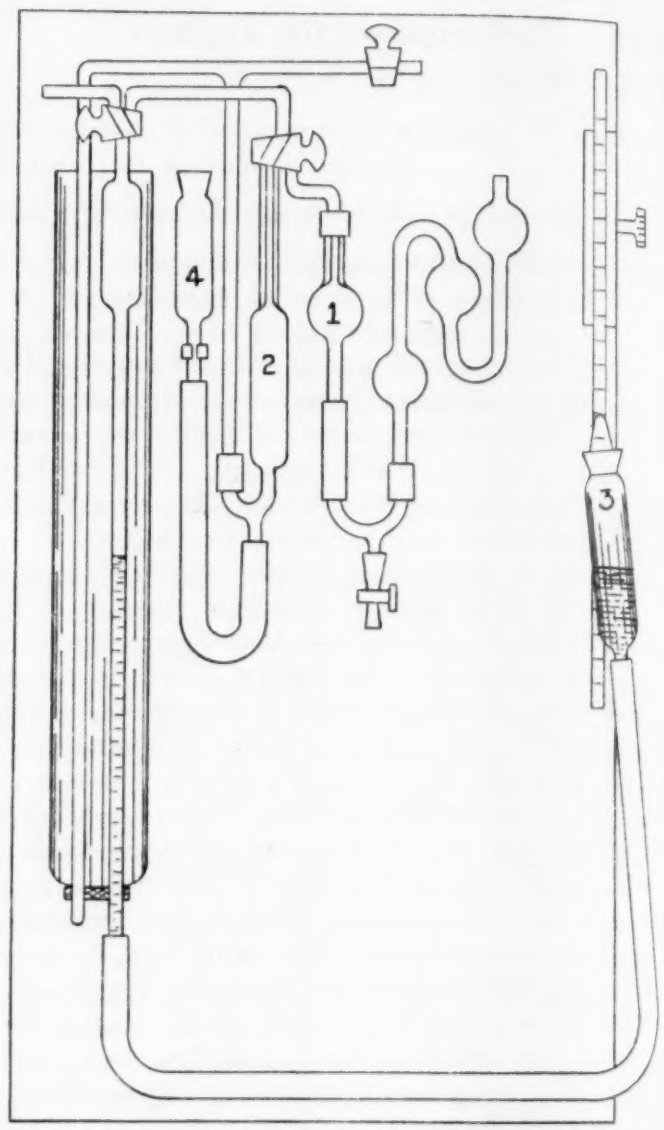

Fig. 1. Oxygen absorption bulb (1), KOH tube for CO_2 absorption (2), mercury leveling reservoir (3), and KOH reservoir (4).

Using this modified Hempel tube, the analysis of a gas sample is much the same as that by the Carpenter method. After CO_2 absorption in KOH solution, the gas sample is passed into the "Hempel" tube. The stopcock to this tube is closed, and the tube is shaken for about 10 seconds. This procedure is repeated 6 times, a burette reading being taken on the 5th and a check reading on the 6th. Thus, oxygen is completely absorbed after a total of 6 contacts with the pyrogallol solution.

With this improvement, the time necessary for a complete analysis of oxygen and carbon dioxide was reduced from the previous average of 30 minutes to about 15 minutes, a time decrease which looms more significant as the number of analyses increases.

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[1] The authors gratefully acknowledge the technical assistance of Milton Folawn.

A Mercury Switch for Thermocouples

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During the recent national emergency, when materials for research either were not available or were difficult to obtain within a reasonable period of time, the need arose for a switch which would automatically and alternately close each of two thermocouple circuits connected to a single recording potentiometer. Such a switch must be so constructed that the contact points do not become fouled, thus creating electrical resistance. To meet this need, the mercury switch described below was constructed and found to operate efficiently.

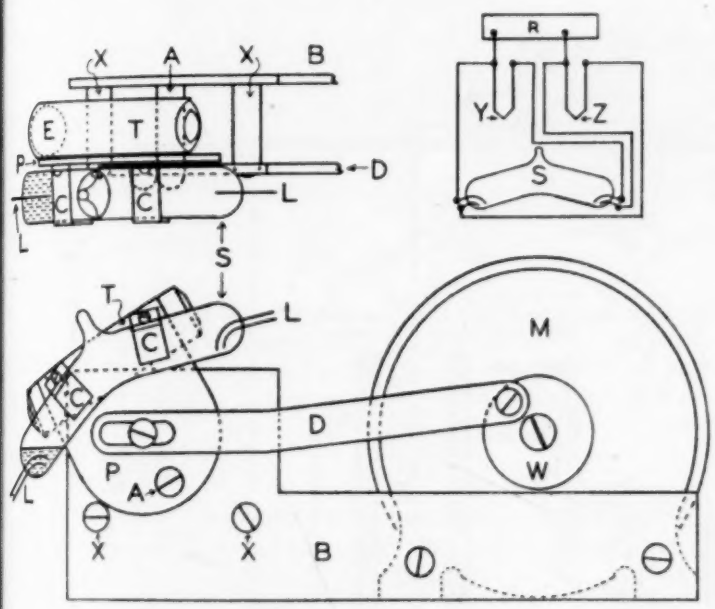

FIG. 1

The switch proper (S) was made from a piece of 12-mm. soda-lime glass tubing, 65 mm. in length and bent to form an angle of about 150°, as shown in the front and top views in Fig. 1. Two platinum lead wires (L) were sealed into the ends of the switch as indicated. A minimum quantity of distilled mercury was placed inside the tubing to insure that the two lead wires at one end would be adequately covered and, thus, the circuit through them closed. The glass switch was evacuated and sealed off as shown.

The switch (S) was mounted by means of two small brass strips (C) to a brass plate (P), mounted on a brass base (B) by means of a pivot (A) which was made of a brass collar on a 1-inch, No. 10, 32-thread brass machine screw. The plate (P) and the base (B) were made of $\frac{1}{16}$-inch sheet brass.

In order to change from one thermocouple circuit to another, the driver (D), made from $\frac{1}{16}$-inch sheet brass, was attached to the driving wheel (W) on the shaft of a 1-r.p.m. motor. Obviously, any desired period of time for each circuit may be obtained by using a motor (M) with the desired r.p.m. or suitable reduction gears on an available motor. On this switch a Speedway motor,[2] No. 953-W, for 110-volt, 60-cycle alternating current, having a shaft speed of 1 r.p.m. was used. This afforded a 30-second cycle for each thermocouple circuit.

To insure the quick breaking of one circuit with the simultaneous quick closing of the second circuit, a steel ball (E), $\frac{3}{8}$ inch in diameter, was placed inside a $\frac{1}{2}$-inch brass tube (T), $1\frac{3}{4}$ inches long. The ends were crimped and the tube soldered on the back of the brass plate (P) as shown in Fig. 1. The extent to which the switch may be thrown in either direction is governed by the studs (X) upon which the brass plate (P) rests. These studs were made in the same manner as the pivot (A) previously described.

The wiring diagram for the thermocouple circuit is shown in the upper right-hand corner of Fig. 1. The two thermocouples are indicated by Y and Z; the recording potentiometer by R.

Very satisfactory results were obtained using this switch with one recording potentiometer to determine the temperatures of the heads of two gas fractionating columns operating simultaneously.

[1] The author is indebted to A. E. Wood for suggested improvements in the original design of this switch.

[2] Manufactured by the Speedway Manufacturing Company, 1834 South 52nd Avenue, Cicero, Illinois.

Carbon 14 Production From Ammonium Nitrate Solution in the Chain-reacting Pile[1]

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It may be of interest to describe the method of production of the radioactive C^{14} currently being released by the Manhattan District in its isotope distribution program. C^{14} was discovered several years ago (*4*), and its general characteristics were correctly determined from weak samples resulting from prolonged cyclotron activation. These characteristics may be summarized as follows: (a) a half-life estimated as some thousands of years; (b) no gamma rays; (c) beta particles with a maximum energy of 0.14 Mev. In addition, it had been ascertained that C^{14} results from the reaction of neutrons with nitrogen—$N^{14}(n,p)C^{14}$, and that this reaction takes place under the action of slow neutrons (*1*). The latter property has become a particularly fortunate one since the advent of chain-reacting piles, with their great abundance of slow neutrons. Its significance is twofold: in the first place, samples thousands of times stronger than those which were made with great patience with the best cyclotrons can now be produced with relatively little effort, and, secondly, the C^{14} which results is (at least in theory) isotopically pure, since no other carbon is involved in the manufacturing process. Thus, a high level of specific activity is obtainable—always an important consideration, but particularly so when very long half-lives are involved.

Thus, the problem of manufacture becomes one of irradiating nitrogen in the pile and of subsequently separating the carbon. Although there are many ways of doing this, the choice is narrowed by practical considerations. For example, space economy demands that the nitrogen be in some form of high atomic density, and neutron economy demands that it should not be combined with elements which would contribute high parasitic neutron absorption. Furthermore, the nitrogen must not be in the form of a compound which will decompose

[1] Work done under the auspices of the Manhattan District.

[2] The assistance of E. P. Meiners, Jr., Miss T. I. Arnette, and F. Schuler is gratefully acknowledged. We consider ourselves honored to have been associated with the late Dr. Louis Slotin in the early phases of the work.

badly under the radiation present in the pile. Also, the material should not contain, in combination or as impurities, elements which would lead to conflicting radioactivities such as would require special decontamination procedures.

In our case, considerations of expedience also were important. At the time of the start of the work the occasion demanded an apparatus on the laboratory scale which would produce significant amounts of C^{14}, which would employ only readily available materials, and which would avoid the laborious process of "canning" material in welded aluminum jackets prior to irradiation. With these factors in mind, we chose to take advantage of the high water-solubility of ammonium nitrate and to build a solution "factory" which would work on the principle of continuous extraction. It was to be expected that most of the C^{14} would be evolved from such a solution in the form of gaseous compounds (*4*). Also, it was known that the decomposition of the solution by the radiation in the pile would produce a gentle stream of gaseous products, which might automatically provide a means of carrying the C^{14} out of the solution.

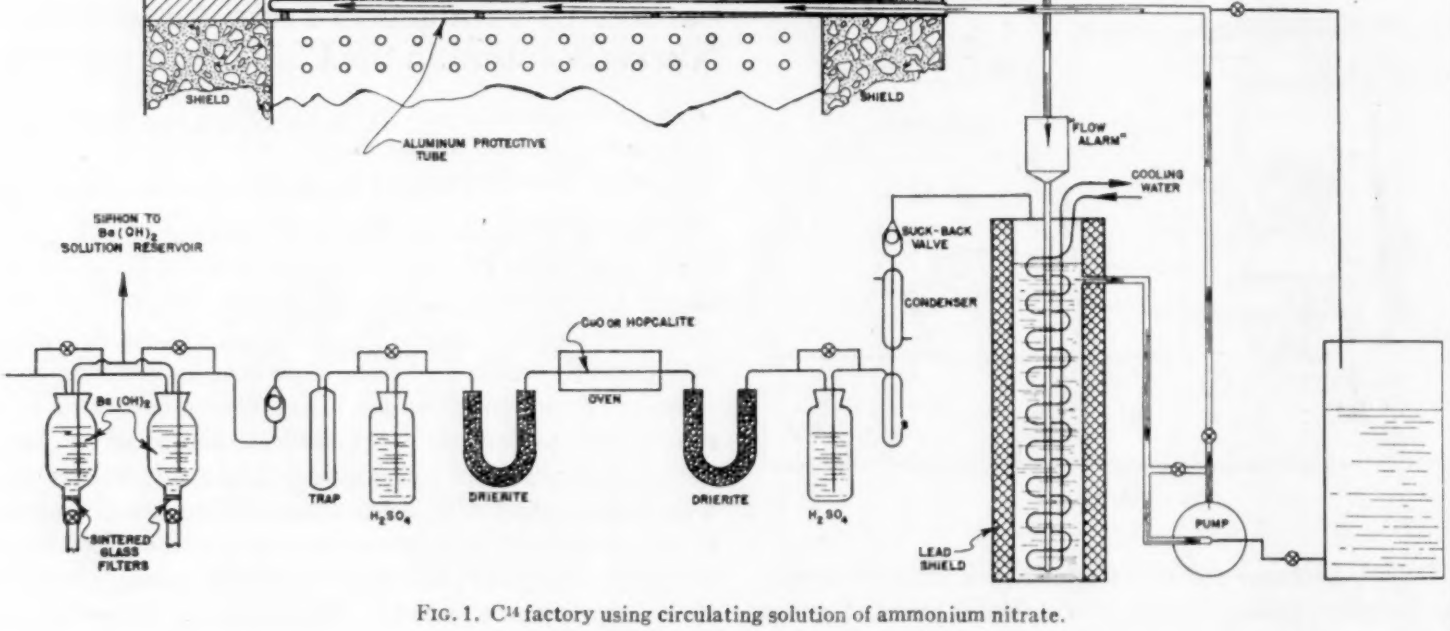

FIG. 1. C^{14} factory using circulating solution of ammonium nitrate.

The apparatus diagrammed in Fig. 1 was constructed upon a design intended to make the most of the automatic carrying and automatic purification inherent in these considerations. A glass centrifugal pump circulated the ammonium nitrate solution through a U-tube in the pile and then through a tall, lead-shielded vessel which served two purposes: (1) to provide a venting-off point for the gaseous products, and (2) to act as a heat exchanger so that the NH_4NO_3 solution might be cooled. A reservoir (shown at extreme right of figure) was used for occasional replenishing of the liquid or for storing the solution if the factory had to be emptied. The circulating system, constructed of aluminum, stainless steel, and glass, had a total volume of 55 l. The evolved gases which gathered above the liquid in the tall, lead-shielded vessel, were led off through a simple train containing drying agents, oxidizing agents, and, finally, bubblers containing barium hydroxide solution, in which the $C^{14}O_2$ precipitated as $BaC^{14}O_3$.

The factory was operated continuously, requiring only occasional inspection and removal of the $BaCO_3$ precipitate every few days. The gas stream ran at the rate of about 15 cc./minute, and measurements of its radioactivity showed that the extraction train was 99 per cent efficient. W. B. Leslie, of Clinton Laboratories, also analyzed the solution and found small fractions of C^{14} present as HCOOH, CH_2OH, and HCHO. From his data we have ascertained that these fractions comprise about 1 per cent of the total C^{14} collected. As might be expected, there is also dissolved in the solution a small residual amount of $C^{14}O_2$ which can be recovered easily by acidification. Tests also showed that practically no C^{14} was present in the form of the cyanide radical either in the gaseous phase or in the solution.

Mass spectrographic examination of some of the carbon from the factory was carried out by M. G. Inghram, of the Argonne National Laboratories. Dr. Inghram's results are reproduced in Fig. 2. The increase in the intensity of the mass 46 peak in the radioactive sample is quite spectacular. This peak is due mostly to $C^{12}O^{16}O^{18}$ in the normal CO_2 and mostly to $C^{14}O_2^{16}$ in the enriched material. Various considerations preclude the possibility that the increase can be due to disturbances in the normal abundances of the oxygen isotopes such as might, for example, lead to too much $C^{12}O^{16}O^{18}$. Quantitatively, Dr. Inghram's results showed that this sample contained C^{14} in an isotopic abundance of 3.3 per cent. When an absolute beta count was obtained on another portion of this sample, a value of about 5,300 years was obtained (*2*) for the half-life of C^{14}. This was in good agreement with the value of 4,700 years obtained by Reid, Dunning, Weinhouse, and Grosse (*3*) in an exactly analogous experiment with a different sample of C^{14}, which presumably also originated in our factory. For pure

C^{14}, this value of the half-life gives a specific activity of about 5 mc./mg.

The richest samples of C^{14} yielded by the factory had isotopic concentrations of 5.0 per cent. We have no satisfactory explanation as to the origin of the inactive carbon. Although some precautions were taken to remove $C^{12}O_2$ from the solution before charging it into the circulating system, we obtained

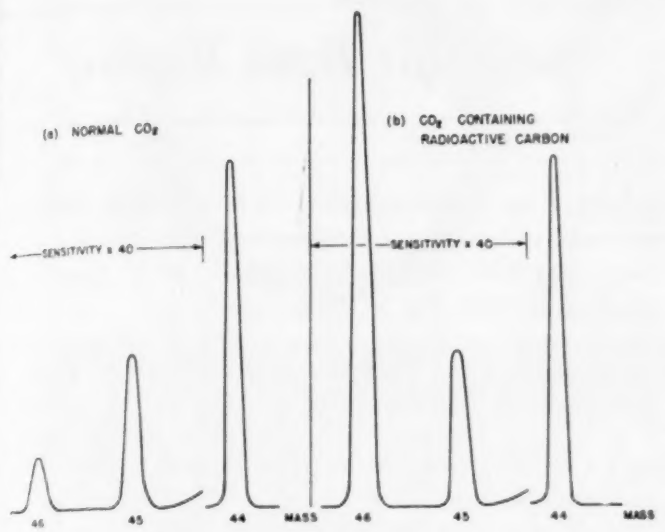

FIG. 2. Mass spectrograms of relevant peaks of normal and enriched CO_2 showing the great increase in the intensity of the mass 46 peak due to the presence of $C^{14}O_2^{16}$ in the enriched sample. The mass 44 ($C^{12}O_2^{16}$) peak is given on a scale equally reduced for the two samples. (Courtesy of M. G. Inghram.)

large amounts of precipitate of lower specific activity during the first few days of bombardment. However, after the first week, the isotopic concentration of our product changed very little with long periods of irradiation, which might be interpreted as evidence that carbonate impurities and residual, dissolved $C^{12}O_2$ in the NH_4NO_3 solution could not be the only source of the inert carbon. We satisfied ourselves that no inward air leaks were present on the suction side of the pump, but apart from making these observations, we did not attempt to increase the isotopic purity; even 1 per cent is ample for almost all tracer experiments, and we were pleased that the specific activity was as high as it turned out to be.

Some 50 mc. of the C^{14} made in this factory have been distributed in lots of 1 mc. or less to research institutions in the United States. The factory has now fulfilled its rather temporary function, and operation is being discontinued in favor of larger-scale production methods. There is a stock pile sufficient to carry over until the new methods come into quantity production. It is to be expected that in a year or so C^{14} will be so cheap and abundant that it will be more in the class of a commodity than that of a novel and treasured substance.

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A New Method of Recording Arterial Blood Pressure

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A simple, accurate, and linear method of measuring intra-arterial blood pressure has been developed. Preliminary work indicates that this apparatus may prove to be of value in the measurement of other intraluminal pressures, such as those within the veins and in the subarachnoid space.

The apparatus consists of a Statham Pressure Transmitter[1] fitted with a short metal coupling which carries any gage needle. The transmitter operates on the strain gage principle and is enclosed in a metal housing measuring 1 x 1 x 3 inches. The input circuit is supplied by a dry cell; the output circuit is connected to the electrodes of any lead of a string-type electrocardiograph.

Before use the transmitter is calibrated against a mercury manometer, and a desirable range of excursion established by adjusting the string of the galvanometer or the input of the transmitter.

The coupling and needle are then sterilized by boiling, the transmitter filled with heparin (10 mg./cc.), and the coupling

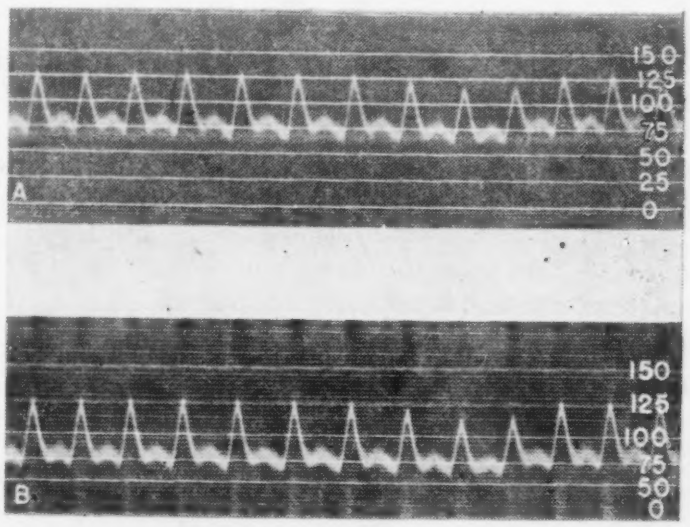

FIG. 1

screwed into place. Enough heparin is displaced by this maneuver to fill the needle. All adjustments having been made, the vessel to be studied is punctured directly, and a photographic record of the movements of the galvanometer string is taken. The photograph in Fig. 1 illustrates a simultaneous recording by this instrument (A) and by the Hamilton manometer (B). The wide horizontal white lines represent millimeters of mercury as marked; the heavy vertical lines, intervals of 1/10 second.

[1] Model P6-6g-250, manufactured by the Statham Laboratories, 8222 Beverly Boulevard, Los Angeles 36, California.

Book Reviews

The Trematoda: with special reference to British and other European forms. Ben Dawes. Cambridge, Engl.: at the Univ. Press; New York: Macmillan, 1946. Pp. xvi + 644. (Illustrated.) $10.50.

This book includes in one volume the more significant information from the literature on the Trematoda. It provides means for identification of the trematode parasites of representative animals of Europe and other countries. The treatment of North American literature on the group, although less complete than that of Great Britain, is extensive. The volume presents a more complete description of the structure, modes of life, bionomics, and life histories of the class than can be found in any single volume hitherto published. While not sufficiently complete to serve as a reference text for specialists on trematodes, it will be valuable to students, teachers, and research workers in their quest for relevant information on the members of this class. More specific information may be obtained from the approximately 1,600 titles cited in the list of literature, detailed references to the authors of which are given throughout the text. In this respect alone the volume is a very important contribution.

After brief treatment of the interrelations of the classes in the phylum Platyhelminthes, the author turns to the Trematoda and contrasts the life histories of Monogenea and Digenea, with examples. The taxonomic position of the order Aspidogastrea is discussed. Detailed descriptions of the external and internal structures in members of the Monogenea and Digenea are given to enable the reader to interpret the material dealing with the taxonomy of these forms. In the section on classification of Monogenea, a key to the suborders, superfamilies, and families is followed by a diagnosis of each group with further keys to the subfamilies under the diagnosis of each family. A similar but more comprehensive scheme is undertaken with keys and diagnoses of 47 families of the Digenea.

Three hundred pages list and describe the Monogenea of British fishes and Amphibia, the digenetic trematodes of British and some other fishes, some common Digenea of Amphibia and Reptilia, and some trematodes of birds and mammals. Many species are described and figured, and keys to genera with diagnoses and lists of species are provided. Many North American forms are included.

The author presents the larval types of the Digenea with descriptions of specific examples and ample illustrations. The different types of life histories of Trematoda are described and their reproduction, geographical distribution, and phylogeny discussed.

The book is stimulating and suggests many opportunities for further research. Particularly is this true in the section on the biology of the Trematoda, where the author introduces some of the problems concerning the fundamental physiological processes of trematode larvae.

A special effort is made to use scientific names correctly and to eradicate the confusion that has in some instances resulted from their misuse. The book contains seven comprehensive tables and hundreds of illustrations, some new and some redrawn from various authors. Cross references appear throughout the text, which is completely indexed.

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Scientific Book Register

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